



RARE DISEASE AND ORPHAN DRUG REGISTRIES

2nd International Workshop
21-22 October 2013
Italian National Institute of Health – Rome (Italy)



RARE DISEASE AND ORPHAN DRUG REGISTRIES

2nd EPIRARE International Workshop

October 21-22, 2013
Italian National Institute of Health
Rome (Italy)

ABSTRACT BOOK

Edited by
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Italian National Institute of Health





NOTE FOR READERS


This workshop has been organised within the framework of activities of the EPIRARE project, which is co-funded by the European Union (EU) Programme of Community Action in the Field of Public Health (2008–2013). The project aims at building consensus and synergies for the development of a EU platform for rare disease registries and at addressing relevant regulatory, ethical and technical issues associated with the registration of rare disease patients in Europe. In the field of rare diseases, cooperation is essential not only at the European level but also at the international and global level. Indeed, in April 2011 the European Commission and the US National Institutes of Health (NIH) successfully launched the International Rare Disease Research Consortium (IRDIRC). Since the launch, the interest to participate has been growing rapidly and many other Countries are joining the consortium.

In this scenario, EPIRARE considered necessary to convene an International Workshop where the scientific community, patients Associations, industry and Institutions, from the EU and beyond, can debate on the use of rare disease registries, on their needs and on the possibility to create common grounds and to share data. This debate is expected to give important inputs to the preparation of a rare disease registry platform that will be considered by the EU, Member States, and possibly by other countries, for integration within the future international cooperation on rare diseases research and public health initiatives.

To this aim, besides the oral and poster sessions presenting the wide and rich experiences of different stakeholders from different Countries, the Workshop program includes a Round Table to debate aims, feasibility and dimensions of a common data set elements shareable among registries. Moreover, a discussion session is scheduled to allow debating on the general features of the rare disease registry platform which is being devised by EPIRARE.

In the meantime, the European Union has started a process of revision of the Personal Data Protection Directive, which has impacted and may still impact dramatically on the multicentre operation of rare disease registries, which have a special need for international and even global dimension. Therefore, the Workshop provides a timely opportunity to disseminate the information and to raise consensus on a petition for amendments of the new regulation on personal data protection, which is currently under scrutiny by the European Parliament.

The EPIRARE project (www.epirare.eu) is co-funded by the European Union (grant agreement n. 20101202). The activities are coordinated by the National Centre for Rare Diseases, National Institute for Health (Italy) and are carried out in association with Institute of Health Carlos III (Spain), London School of Economics and Political Sciences (UK), European Organization for Rare Diseases (France), Scientific Institute of Public Health (Belgium), National Research Council, Institute of Clinical Physiology (Italy), Hellenic Centre for Disease Control and Prevention (Greece), Bulgarian



Association for Promotion of Education and Science (Bulgaria), Maastricht University (the Netherlands), Ministry of Health and Social Policy (Spain) and Ministry of Health, Quality Department (Italy).



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PROGRAM





MONDAY OCTOBER 21, 2013

- 8.00 Registration
- 9.00 Welcome addresses
FABRIZIO OLEARI, MONICA BETTONI
MINISTER OF HEALTH
- 9.15 Aim of the Workshop
DOMENICA TARUSCIO

SESSION I

THE MOVING CONTEXT OF RARE DISEASE REGISTRIES

Chairs: ANTONI MONTSERRAT, DOMENICA TARUSCIO

- 9.30 Future scenarios in the field of rare diseases
ANTONI MONTSERRAT
- 9.50 Toward a European Platform for rare disease Registries
SIMONA MARTIN
- 10.10 The EPIRARE proposal for a European Platform
LUCIANO VITTOZZI
- 10.30 *Break*

SESSION II

THE INTERNATIONAL AND EUROPEAN CONTEXT FOR RARE DISEASE RESEARCH

Chairs: ANTONI MONTSERRAT, DOMENICA TARUSCIO

- 10.50 International Consortium for rare diseases research - IRDiRC
STEPHEN GROFT
- 11.10 E-RARE
DARIA JULKOWSKA
- 11.30 EU research infrastructures
FILIPPO BELARDELLI
- 11.50 Gaps and synergies to develop new treatments for rare disease patients
GIOVANNI MIGLIACCIO
- 12.10 General Discussion
- 12.30 *Lunch break*
- 13.00 **POSTER SESSION**
(*Discussants: SABINA GAINOTTI, EMANUELA MOLLO*)

SESSION III

INTEROPERABILITY OF NATIONAL AND INTERNATIONAL RARE DISEASE REGISTRY PLATFORMS

Chairs: FABRIZIO BIANCHI, RUMEN STEFANOV

- 14.30 Global Rare Diseases Patient Registry
STEPHEN GROFT, YAFFA RUBINSTEIN
- 15.00 The Spanish National Rare Diseases Registry
MANUEL POSADA
- 15.20 The system of French National Rare Diseases Registries BaMaRa-BNDMR-RaDiCo
PAUL LANDAIS
- 15.40 The Italian National Rare Diseases Registry
YLLKA KODRA
- 16.00 The Paroxysmal Nocturnal Hemoglobinuria (PNH) registry
LUCIO LUZZATTO
- 16.20 The future of Rare Diseases registries in the EU: learning from the past
GEORGIOS MARGETIDI
- 16.40 General Discussion
- 17.15 End of the first day
- 17.15 / **EPIRARE MEETING (ONLY FOR EPIRARE PARTNERS)**
19.00

TUESDAY OCTOBER 22, 2013

SESSION IV CASE STUDIES

Chairs: SILVIA MANEA, MANUEL POSADA

- 9.00 The Coordination of Rare Diseases at Sanford (CoRDS) patient registry for all rare diseases
LIZ DONOHUE
- 9.15 The Eurofever registry: update on enrolment after 3 years
MARCO GATTORNO, SILVIA FEDERICI
- 9.30 eurIPFreg: A European Registry and Biobank for Patients with Idiopathic Pulmonary Fibrosis
FOTIOS DRAKOPANAGIOTAKIS
- 9.45 The I-DSD Registry – A forum for international research & professional networking
FAISAL AHMED
- 10.00 TOSCA, TuberOus SCLerosis Registry to IncreAse Disease Awareness: Registry Desi
CARLA FRAWDROSKI
- 10.15 International Registry of Steroid-Resistant Nephrotic Syndrome: updated epidemiological and clinical data
MANUELA CURRERI
- 10.30 Italian Cystic Fibrosis Registry (ICFR) data quality assessment
NATALIA CIRILLI
- 10.45 EUROMAC- European Registry of Patients Affected by McArdle Disease and other Rare Glycogenosis presenting with exercise intolerance
ANDREA MARTINUZZI
- 11.00 EPIRARE Video “Half of a score”
- 11.15 Coffee break
- 11.40 The Law’s Role in rare disease and orphan drug registries: privacy and data
DAVID TOWNEND

SESSION V

CASE STUDIES

Chairs: ANGELA BRAND, OLIVIA SCHREIBER

- 12.00 The Lombardy Regional Registry for Rare Diseases: an example of record linkage across different data sources
GEDEONE BARARLDO, LAURA BOTTANELLI
- 12.15 The disease registries as instruments of knowledge and research in rare skeletal dysplasias
MARINA MORDENTI
- 12.30 Pharmacovigilance using patient registries
JACQUI VAN RENS
- 12.45 Why developing an orphan drugs registry?
VIVIANA GIANNUZZI
- 13.00 Lunch

SESSION VI

CASE STUDIES

Chairs: MONICA ENSINI, LUCIANO VITTOZZI

- 14.00 Issues highlighted by the EPIRARE surveys of rare disease registries
EMANUELA MOLLO, LUCIANO VITTOZZI
- 14.20 Advanced neuromuscular registries
KAREN RAFFERTY
- 14.40 Alpha-1-Antitrypsin International Registry
MAURIZIO LUISETTI
- 15.00 Analysis of the phenotypes in the Rett Syndrome Networked Database
ALESSANDRA RENIERI
- 15.20 Rare diseases and transplantations
ALESSANDRO NANNI COSTA
- 15.40 General Discussion
- 16.30 Conclusion

SPEAKERS AND CHAIRS

FAISAL AHMED	<i>University of Glasgow, United Kingdom</i>
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POSTERS

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N. 1

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

A New International Web-based Registry for Dysferlinopathy Involving Participation of Patients and their Doctors

AUTHORS

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ABSTRACT

The creation of the International Dysferlinopathy Registry is an important step in improving the care and finding treatments for those affected with a dysferlinopathy. The International Dysferlinopathy Registry, launched in March 2013, is available at www.dysferlinregistry.org in seven languages (Spanish, English, French, Japanese, German, Italian and Catalan). This registry is open to all patients worldwide affected with a dysferlinopathy, including the most frequent clinical presentations – namely Limb Girdle Muscular Dystrophy type 2B (LGMD2B) and Miyoshi Myopathy – as well as all other clinical presentations related to mutations in the dysferlin gene. Registration with the International Dysferlinopathy Registry is initiated by the patient, but also requires participation of their medical doctor(s). Patients register online by self-report after giving informed consent. To initiate their registration, patients are asked to provide some personal details and contact information for doctor(s) involved in the diagnosis and follow-up of their disease, as well as give consent. While the registry curator then contacts the medical doctor(s) to obtain the genetic and biological data (mutation in dysferlin gene, as well as dysferlin and CPK protein levels) needed to confirm the registration, patients are invited to connect to their personal user account in order to complete an online secure medical questionnaire. This questionnaire consists of 30 easy-to answer questions related to the patient's diagnosis, disease onset, family history, motor, cardiac and respiratory functions, medical treatment(s) and participation to research studies or clinical trials. The patient's registration is validated after the patient has completed his/her medical questionnaire and once the registry curator has confirmed the patient's eligibility (i.e. at least one pathogenic mutation identified in the dysferlin gene). Members of the International Dysferlinopathy Registry will receive information relevant to their condition, such as whether they might be suitable for certain clinical trials or research studies (such as the International Clinical Outcome Study for Dysferlinopathy), as well as about better ways of caring for patients with a dysferlinopathy once those ways are identified. Data collected in this registry will help researchers to be better equipped for finding therapies for this disease, to understand how many people worldwide are affected by this rare condition and what the precise genetic defects are, and will help to support other activities to improve patient care, such as assessment and dissemination of standards of care. In addition, third parties can request anonymised medical data from the registry and – subject to approval – use the obtained information for research, study/trial feasibility or planning, or patient recruitment into clinical studies/trials. To facilitate the combined use of phenotypic data, biosamples and –omics data for rare disease research, the Registry will work with the EU project RD-Connect to implement a Global Unique Identifier for patients and implement standardized coding systems and ontologies.

N. 2

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

European Database for Myasthenia Gravis: an international disease registry

AUTHORS

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ABSTRACT

Myasthenia Gravis (MG) is a rare and heterogeneous neuromuscular disease leading to abnormal fatigability of various muscles; MG affects about 20 per 100,000 people worldwide and shows an increasing incidence. A European Network on MG, supported by EU (EuroMyasthenia Network, EU-2005105, DG SANCO, and Fight-MG project, HEALTH-F2-2010-242210), was established in order to built up a multidisciplinary team focused on this disease; the development of a database specific for MG patients living in Europe (EuroMG-DB) was among the objectives. The EuroMG-DB was developed in 2007, aiming to collect relevant information from local ongoing MG registries and clinical records. The EuroMG-DB was designed with a flexible structure for continue implementation. Referring physicians are responsible for collecting the patient's data, in accordance to local Ethic Committees and National laws on personal data protection. The EuroMG-DB is accessible via an encrypted Client – Server protocol, allowing a real time data entry; quality control on the data is assessed in order to guarantee reliability of the database itself. 2500 clinical records have been gathered from 6 European MG referring-centres. The EuroMG-DB can interact with Business Intelligence applications to provide specific and rapid analysis on the data, focusing on the main MG clinical features (i.e. sex distribution, grouped by disease onset, or disease severity at the first visit, at maximal worsening, and at the last visit, grouped according to the referring clinical centers). Collection of clinical and immunological information aims to improve our knowledge on MG; however, large numbers of data are still required, especially for clinical and epidemiological research. Widening the use of the EuroMG-DB across Europe will provide more accurate information about the MG population, highlighting local differences in disease manifestations, response to therapies, and improving clinical research to individualized MG treatment. Our experience indicates a way to collect data from different locations fulfilling the expectations on the use of such registries. The EuroMG-DB has been developed in collaboration with some of the MG clinical centers in Europe, and will collect information from the majority of MG patients living in EU, overcoming national barriers. The EuroMG-DB is supported by the European Commission - FIGHT-MG project (HEALTH-F2-2010-242210).

N. 3

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

The RAM-NET Registry for neuromuscular diseases, a strategic tool for research and trial readiness

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ABSTRACT

Rare disease registries begin to be recognised as important tools in support of clinical experimental research. Their implementation is essential for building trial readiness and requires the effort and cooperation of patients and organisations on one side and clinical investigators on the other. In the field of neuromuscular disorders (NMD), several initiatives exist both at the Italian and international levels (see www.treat-nmd.eu for an overview). One of these is the Italian NMD registry (RAM-NET, www.registronmd.it), a web-based informatics platform that hosts disease-specific databases for different NMD. At the moment, these are: DMD, SMA (both based on self-reported forms) and Charcot-Marie-Tooth disease (CMT) database (which requires specialist's support of for data collection). The platform design, however, will allow further expansion to incorporate new disease-specific databases. In addition, RAM-NET provides information on Telethon prospective research Registries developed by clinicians on other muscular dystrophies and mitochondrial diseases. The governance of the Registry is based on a legally recognised entity responsible for data management and storage according to the Italian laws on data protection. It includes the following Italian patient associations: AISLA (ALS association); ASAMSI and Famiglie SMA (SMA associations); UILDM (MDA association); ACMT-Rete (CMT association) and Fondazione Telethon. All partners contribute to cover Registry's maintenance and activities costs. An independent Ethics Board provides support on ethical issues and regulates the access of the scientific community to the de-identified data. The registry is linked to international initiatives such as the Treat-NMD Global Registry (for DMD and SMA) and the Inherited Neuropathies Consortium International Registry (Rare Disease Clinical Research Network, NIH, South Florida, USA) for the CMT database. The DMD and SMA registries have already been used to reply to several industry enquiries aimed at setting international trials on these diseases. Moreover, they contributed data to the Global Registry for the preparation of manuscripts on DMD (1) and SMA (2). While self-reported databases proved already their usefulness for the preparation of clinical trial protocols and to identify suitable patients for trial recruitment, their efficacy may be more limited if the data collection has a different research purpose and is oriented, for instance, at capturing detailed information on medical history, functional status or any other medical problems. In these cases, the stringer review of clinical and molecular data is essential to guarantee the validation and usefulness of the registry and involves clinical experts. Benefits to patients include being connected with specialists that provide best standards of care and information regarding upcoming trials, while investigators are facilitated in the collection of accurate data for prospective studies. These registries also present several issues. First of all, the key for their success lies in the trust and alliance on a common intent between patients and their physicians. Also, commitment and time/resources availability, long term sustainability, clear rules regarding priority of access to data, etc. are important aspects that cannot be ignored. Nevertheless, it is envisaged that this type of data collection will be more and more critical also for clinical trial, because it will allow to identify suitable patients based on more accurate information, with also an important ethical implication regarding patients' and families' expectations.



REFERENCES

1) Bladen CL et al. The TREAT-NMD Duchenne muscular dystrophy registries: conception, design and utilisation by industry and academia. *Human mutation*, 2013, in press. 2) Mapping the differences in care for > 4000 Spinal Muscular Atrophy patients, a survey of 22 national registries. Manuscript in preparation

N. 4

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

A new project for rare diseases: the Italian National Registry for Myotonic Dystrophies type1 and 2

AUTHORS

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ABSTRACT

Myotonic dystrophies (DM) are considered the most variable neuromuscular disorders in terms of age at onset, severity and different body systems affected. Despite they are rare diseases, in Italy these progressive genetic disorders affect at least 9000 patients (8000 with DM1 and 1000 with DM2), largely undiagnosed. The most pronounced characteristic of DM is skeletal and smooth muscle dysfunction but, in addition to muscle complains, greatly variable symptoms (as cardiovascular dysfunction, respiratory insufficiency,, endocrine deficiency, vision impairment, gastrointestinal disturbances, fertility issues, reduced cognitive function and personality abnormalities) can be present. There is currently no cure for myotonic dystrophy, but there is a lot that can be done to improve patients' quality of life. The value and usefulness of Registries for rare diseases to advance research and knowledge of DM, in the aim of a common gold-standard of care and treatment, has been largely demonstrated worldwide. To improve their lives, italian patients of those living with DM can now join the new Italian Myotonic Dystrophies Registry that can rely on a network of sixteen centers, throughout Italy, coordinated by IRCCS Policlinico San Donato, The Registry enrolls individuals throughout Italy who have DM and who are interested in hearing about research updates and studies that they may be eligible to participate in. The participation is voluntary and charge free. The project of the National Registry started on December 2012. The approval of the ethics committee has been obtained in July 2013 and the patient's enrollment will start in August 2013. A specifically dedicated website (www.distrofiamiotonica.it) has been created in which DM patients (or their tutors) and researchers will be allowed to fill records of molecular, clinical and with regard to the quality of life data. There are two different data entry levels: patient form and physicians form. The individual information will be kept completely confidential. Patients can opt out of the Registry at any time. Because of the range of systems affected, management requires an expansive approach and care is best provided by a coordinated, multidisciplinary approach. Therefore the Registry contains twelve different sheets to characterize the multisystemic involvement of DM; each sheet includes qualitative and quantitative informations. Some of the requested items are mandatory to harmonize the data collection for international sharing. The National Registry will create a large, clinically and genetically well-characterized population of DM 1 and 2 Italian patients and will advance research in DM by helping patients to participate in clinical studies. The Registry's main goals are to advance research and knowledge of myotonic dystrophies (DM).



REFERENCES

www.fondazioneemiladistromiotonica.org/ www.distrofiamiotonica.it

N. 5

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

The potential of population-based registries in assessing and controlling the impact of inherited coagulation disorders in the community

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ABSTRACT

Inherited coagulation disorders are a group of RD, whose affected patients need complex, highly specialized care. In the framework of the Italian legislation on RD, Regional Health Authorities have identified Centres of expertise for ICD, in charge of providing comprehensive and multidisciplinary care, and have established registries, to trace patients' health care pathways and able to monitor treatments and outcomes. The experience of the Veneto region in this field is presented. Data from the RD Regional Registry, monitoring a population of 4.9 million inhabitants and referred to the period 1st June 2002- 1st June 2013 are presented. Patients affected by a RD at 1st June 2013 were 23,952. Of these, 15.7% were affected by rare haematological conditions, representing the second most frequent group of RD monitored by the Registry. Of these, 1.701 (45.2%) were recorded as having an inherited coagulation disorder. Among the group the diagnosis' distribution is the following: haemophilia A (29%), haemophilia B (4%), haemophilia C(1%), von Willerbrand disease (44%), other coagulation defects (21%). Approximately 13% of the total patients are pediatric patients. Comparing these data with the ones derived by the Hospital Discharge Records Registry we achieve a high level of coverage of patients affected by ICD (98%). Furthermore, it comes out that Centres of expertise of The Veneto Region have a high attraction rate (14%). In a three years period these patients have experienced a global amount of 1.388 hospital admissions, with a median Length of Stay (LoS) of 6 days. The therapeutic plan of each recorded patient is recorded in the Registry through an on-line tool used by prescribing clinicians and pharmacists delivering treatments to patients. A total of 919 therapeutic plans, which include all the prescriptions (n=1021) issued to these patients, were managed by the Registry. The Registry represents a very useful tool able to describe patients' natural histories and outcomes, as well as access to care. From the Regional Health Authority perspective it represents a powerful tool to monitor prescription habits and Centres' activities. Recently, an Agreement between the State and the Regions regarding the definition of regional/interregional care pathways for ICD patients has been approved. Data from the Registries established at regional/interregional level can support the implementation of the Agreement and serve as powerful monitoring tools, with the aim of supporting health care planning and guaranteeing a high standard of care to patients.

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N. 6

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

A patient-initiated registry for Rare Diseases: the experience of the Greek Alliance for Rare Diseases (PESPA)

AUTHORS

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ABSTRACT

INTRODUCTION: The Greek Alliance for Rare Diseases (PESPA) was founded in 2003 by representatives of patient associations, scientists, clinicians, with the support of EURORDIS. Its objective was to create a focal-point for all rare disease (RD) patient associations in Greece, as well as RD patients. Amongst primary goals is the creation of a Greek RD registry. Following intensive lobbying by PESPA, a Greek National Plan for RD was formatted by the Ministry of Health in 2008, including initiation of a National RD registry. As a result of the Marianna Lambrou's continuous effort, PESPA will collaborate with the University of Athens School of Medicine in order for its registry to be officially recognized. **METHODOLOGY:** To fulfill legal and ethical requirements when recording personal information, PESPA acquired a license for private-information-data-collection from the Hellenic-Data-Protection-Authority (30/09/2008; GN/EX/587-1/30-09-2008). Following informed consent by patients (or parents in case of minors), data were collected based on a questionnaire developed by PESPA. Information included: RD diagnosis, responsible clinic/physician, patient identification (coded), age, disease history, geographical origin, etc. **RESULTS:** Currently twenty-six patient-organizations are affiliated with PESPA, representing ~8,000 patients. The largest are for Cystic Fibrosis, Retinopathies, Sickle-Cell Anemia, Tuberous Sclerosis, Lysosomal diseases, Congenital Heart Disease, Myopathies and Hemophilias. To date, >1.000 individual patients have been registered in the database, corresponding to 300 RDs, without being a member of an association. Based on database information, PESPA supported the establishment of 2 new patient associations (Neurofibromatosis and Hereditary Angioedema). **DISCUSSION:** In the absence of a National RD registry, the data presented here represent a first attempt towards registration of all RDs in Greece, indicating the spectrum of RDs and a preliminary estimate of the numbers of RD patients. Furthermore, this dynamic RD registry can support networking of RD patients, and constitutes a valuable resource for epidemiological studies and clinical trials.

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ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

European registry and network for intoxication type metabolic diseases (E-IMD)

AUTHORS

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ABSTRACT

Organic acidurias (OAD) and urea cycle defects (UCD) are rare intoxication type metabolic diseases (IMD) with overlapping phenotype. Clinical presentation includes acute metabolic decompensation during catabolism as well as acute and/or chronic dysfunction of brain, heart, kidneys, liver, and skeletal muscle. Patients risk death during metabolic decompensation as well as severe disability, impaired quality of life and reduced life expectancy. Individual centres have limited experience and it is therefore necessary to pool resources for collaboration. The European registry and network for intoxication type metabolic diseases (E-IMD, EAHC 2010 12 01; 2011-2013) has been financed by the DG Sanco and is a network of expert metabolic centres, sharing a registry, producing guidelines, best practice, quality assessment, training and tele-expertise. The network includes 79 partners from 23 countries. E-IMD and UCDC (USA) have established a strategic alliance for transatlantic collaboration. E-IMD also works together with other consortia such as the J-UCDC (Japan), SSIEM, patient advocacy groups, and industry. The patient registry is one of the major tasks to improve evidence base and knowledge on these rare diseases (www.eimd-registry.org). Over 600 patients are followed, to date, making it the largest ever cohort of patients with OAD and UCD. It is designed in a modular way containing a core dataset for all IMD to facilitate research across disease areas. Additional individual datasets are elaborated according to disease-specific requirements to address specific research questions for single diseases and disease groups. The registry is designed to collect longitudinal data so that the disease course of individual patients, birth cohorts and disease groups can be easily followed over time. The regular follow-up of patients includes baseline, annual, and emergency visits; the circumstances of fatal disease course are also reported. This visit structure is highly relevant for clinical trials, a precise description of the natural history, rare disease variants and disease modifiers, and the development of evidence-based new treatments and protocols of care, particularly in very rare diseases such as NAGS deficiency where only 2-3 new patients may be diagnosed, per year, in Europe. In 2013, the platform was extended to include patients with homocystinurias and methylation defects (E-HOD - EAHC 2012 12 02). In 2014, we plan to continue clustering of IMD by inclusion of additional diseases, covering 49 IMD in total. Our vision is to expand the registry and network step by step to include all IMD. There are more than 500 known different IMD.

N. 8

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

European network and registry for homocystinurias and methylation defects (E-HOD)

AUTHORS

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ABSTRACT

Patients with homocystinurias (HCU), methylation defects (MD) and folate defects (FD) have an enormous need for improved medical awareness, optimisation of the diagnostic process and therapy, and improved networking between healthcare professionals and patients. An initiative named "European network and registry for homocystinurias and methylation defects (E-HOD)" funded by the European Commission DG Sanco (EAHC 2012 12 02) began in February 2013. E-HOD has 32 partners from 21 countries linking healthcare professionals, patient's representatives and industry. The overall aim of E-HOD is to promote health for children, adolescents and adults affected with these rare and severe diseases. It is our aim to reduce variation between countries and allow patients, wherever they live, to access the necessary expertise and services. E-HOD has three specific objectives: 1) improving knowledge on homocystinurias (HCU) and methylation defects (MD) through the collection of clinical data into a registry, 2) developing diagnosis and clinical care recommendations, 3) evaluating the newborn screening programme with recommendations. E-HOD adds value to the reflection on EU reference networks and registries as it clusters 15 rare diseases onto an existing network and registry (E-IMD) of 11 intoxication type diseases (E-IMD is funded by the EC EAHC 2010 12 01). It also adds value to the reflection on NBS programmes as only 7 European countries have established HCU screening using varying methodology. E-HOD is unique as no other registry or network exists for these diseases. Following the EMA/EUCERD discussions on the need to develop a unique source of data by disease, E-HOD will lead the way in building a registry, with improved sustainability, for researchers, patients, patient organisations, regulators, payers and for orphan drug follow-up through a strategy to develop public/private partnerships. The registry will have a mechanism for reporting drug adverse events. Given the particularly low number of patients and the complexity of the diseases, no national or regional project in Europe would be able to perform this work. The registry will be web-based and allow new partners to join the network and thus the project will allow continuous expansion.

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ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

The TREAT-NMD Care and Trial Site Registry - A powerful tool to improve clinical research in Rare Disease

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ABSTRACT

General information and background: As one branch of TREAT-NMD (EU funded network of excellence, FP6) the Care and Trial Site Registry (CTSR) was established in 2007 as a registry of specialist neuromuscular (NMD) clinical centres which are seeing patients with NMDs and have the necessary facilities and expertise to run clinical trials in NMDs. The CTSR is an online self-registration database hosted by the University Medical Center Freiburg, Germany. The CTSR technical platform comprises a Java web application running on a MySQL database accessed via a secure web server. This allows swift self-registration and update of information by any web browser, regardless of geographic location. Once registered, data is entered into online forms organised by topic categories such as Patient Cohort, Diagnostic Tools, Care Settings, Clinical Trial Infrastructure and Research and Education. With a user agreement each registered site can define the purpose for which their data may be used. For any enquiry the database can be searched using defined search criteria (e.g. number of patients with a specific disease, previous experience with clinical trials). Results: By May 2013 the CTSR contains 280 sites in 43 countries with a total of ca. 39.150 NMD patients reported. Since 2007 the CTSR received 12 requests for feasibility information from industry and academic institutions, some in combination with the TREAT-NMD patient registries. Within the CARE-NMD project (2010- 2013, funded by DG Sanco) the CTSR was extended with Duchenne specific care questions and used to evaluate current clinical practice in different European countries. In 2012 the CTSR helped the Muscular Dystrophy Campaign in United Kingdom to conduct an audit of UK sites to gather accurate baseline data on current neuromuscular provision. Conclusion: The original plan of the CTSR to become a single point of access for pharmaceutical industry and investigators for feasibility and trial site selection has proven to be successful. For sites the CTSR does reduce work load because they do not have to respond to the individual feasibility questionnaires by industry. For industry and academic researchers the CTSR provides a single point access to a worldwide network of neuromuscular centres. The CTSR approach is currently extended to Neurodegenerative Diseases within the Neuromics project (FP7, 2012-2017) and also applicable to other Diseases. It provides a powerful infrastructure to improve clinical networking and research in Rare Diseases.

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www.treat-nmd.eu/ctsr

N. 10

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

German Network for congenital uro-rectal malformations (CURE-Net)

AUTHORS

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ABSTRACT

Background/Purpose: Anorectal malformations (ARM) and the exstrophy-epispadias complex (EEC) are rare forms of congenital uro-rectal anomalies with a worldwide prevalence of approximately 2-4 ARM in 10,000 live-births and 1 EEC in 10,000 live-births. They represent an enormous challenge in the medical care of patients and their families. Despite successful surgical operations, many patients experience long-lasting problems, including incontinence, sexual dysfunction and psychosocial problems. To improve quality of life of patients and to research the causes for ARM and EEC, the German Network for Congenital Uro-RECTal malformations (CURE-Net) was established in 2009. Methods: Affected patients of all ages are identified and recruited through participating departments of pediatric surgery and urology throughout Germany and the German self-help organisations SoMA e.V. and Blasenexstrophie/Epispadie e.V.. Exposures of interest were ascertained through standardized questionnaires. Blood samples were collected for molecular interventions. Results: Extensive epidemiological, clinical and psychosocial data were collected of more than 690 patients and families, including over 265 newborns (~25% of all affected newborns/year) between 2009 and July 2013. In addition, more than 1,100 blood samples were collected during the same time. First results showed great differences in treatment of patients and a lack of data quality especially in older patients. The need of a structured aftercare of affected patients, ideally beyond the adolescent age, is required. To enable this, the first aftercare booklet for ARM was developed in 2013 based on available CURE-Net data. Another booklet for EEC will follow. Evidence on risk factors for both malformations is still sparse. However, molecular interventions showed for the first time a causal microduplication 22q11.2 in EEC patients. Further new causal microduplications and microaberrations in ARM and EEC were observed, but replication of the results is needed. To assess potential environmental risk factors, data of newborns not older than one year after birth were used to minimize a possible recall bias from the parents. First results, such as an increased risk for ARM and EEC after assisted reproductive techniques, indicate a common background with fertility problems/hormonal disorders of the parents. To elucidate underlying mechanisms further detailed analyses are required. Conclusion: No mandatory recruitment of ARM or EEC patients exists in Germany. However, CURE-Net expanded to the greatest interdisciplinary data collection for both malformations in Europe and supports the establishment of reference centres. An important role within the network plays the self-help organisations with their years of experience from the everyday life of patients.

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N. 11

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

More than a single disease registry – The NZ Neuromuscular disease registry

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ABSTRACT

The NZ Neuromuscular disease registry is a national registry with approval to collect information for a range of hereditary and acquired neuromuscular diseases with multiple and varied datasets according to disorder [1]. The primary aim of the registry is to facilitate the recruitment of patients into research. Due to the rarity of disorders covered by the registry it connects to numerous international registries and works to meet the differing requirements of each. Various web-based platforms are used to achieve this including the Neuromuscular Disorders registries that have been developed in collaboration with the Office for Population Health and Genomics (Western Australia) and Centre of Comparative Genomics (Murdoch University Western Australia) [2] and the Charcot-Marie-Tooth disease database developed by the Rare Diseases Clinical Research Network. Behind the registry's commitment to multiple neuromuscular diseases is its close association with the Muscular Dystrophy Association of NZ (MDA NZ). The registry is a shared initiative of the MDA NZ and interested clinicians, receives funding through the research arm of the charitable association and has undertaken to enrol people with any of the conditions supported by the MDA NZ, which includes muscular dystrophies, spinal muscular atrophies, hereditary neuropathies, inflammatory myopathies, myasthenic syndromes and inherited ataxias.

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N. 12

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

INSIGHTS-IPF: Situation of Patients with Idiopathic Pulmonary Fibrosis

AUTHORS

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ABSTRACT

Idiopathic pulmonary fibrosis (IPF), a manifestation of chronic progressive fibrosing interstitial pneumonia, presents with a prevalence of 2-29 cases per 100,000 individuals and thus is a rare disease. Current treatment options are limited, and the mean survival time of the newly diagnosed (mostly elderly) patients is only about 2-3 years. To date, in Europe data are limited on the characteristics and management of such patients. The registry "Investigating significant health trends for patient with idiopathic pulmonary fibrosis (INSIGHTS-IPF)" was initiated by an academia-based expert group end of 2012 for the documentation of incident and prevalent patients with confirmed IPF diagnosis. To avoid selection bias, no explicit exclusion criteria were stated. Quality measures include plausibility checks upon data entry, queries and on-site monitoring with source data verification. Detailed data on patient characteristics, diagnostics, management, clinical outcomes, quality of life and resource utilization are recorded. Visits are documented about every 6 months, and in addition if complications occur (hospitalisation, therapy escalation, exacerbations). A focus of the study is on health related quality of life, and several validated questionnaires are filled out by patients once a year (EQ-5D and WHO-5 as generic instruments; St. George Respiratory Questionnaire (SGRQ) und der University of California San Diego Shortness of Breath Questionnaire (UCSD SoB) for respiratory disease). Data are collected internet-based on Secure Socket Layer (SSL)- and password-secured internet site using a MySQL database, the analysis with SPSS. It is planned to document at least 500 patients in 20 centres (currently 250 patients have been included). The registry will contribute to the optimization of the management of IPF patients in the long term. The Core Recommendations on Rare Disease Patient Registration and Data Collection as adopted by the European Union Committee of Experts on Rare Diseases (EUCERD) in June 2013 will be implemented in the further course of the registry. INSIGHTS-IPF is supported by an Unrestricted Educational Grant by Boehringer Ingelheim, Germany. ClinicalTrials.gov Identifier: NCT01695408.

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N. 13

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

Cerebellar-Brainstem Congenital Defects: why an Italian register for these rare diseases is needed

AUTHORS

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ABSTRACT

Cerebellar and brainstem congenital defects (CBCDs) represent a heterogeneous group of disorders with major consequences in terms of mortality and morbidity. Recent advances in genetic and neuroimaging technology have greatly advanced our understanding of these malformations. Primary CBCDs are estimated to affect about 1 in 5000 live births, yet their prevalence at conception is expected to be much higher, given that foetal posterior fossa defects are among the most commonly diagnosed brain malformations in utero. The clinical presentation of CBCDs can be extremely variable. Along with cerebellar signs such as ataxia and nystagmus, visual problems are frequent, as well as mental retardation and other cognitive and behavioural dysfunctions. A subset of patients are syndromic, and the neurological phenotype related to the malformation can be variably associated with dysmorphic features and/or multiorgan involvement. In recent years, progress has been made in understanding the genetic basis of some mendelian CBCDs. The most representative are the recessively inherited Joubert syndrome and related disorders (JSRD), a group of conditions sharing a typical neuroradiological malformation termed "molar tooth sign" (MTS) associated with neurological signs and variable multiorgan involvement mainly of the kidneys, retina and liver. To date, in the vast majority of CBCDs, the aetiology remains unknown. Despite developments in genetics and neuroimaging that have improved the diagnostic rate of CBCDs, these rare disorders are still underdiagnosed and poorly understood. A better knowledge of these conditions will raise the general awareness of them in the medical community, providing direct benefits to the patients and their families through: (1) diagnostic, carrier, and prenatal testing; (2) more accurate information about prognosis and recurrence risk; (3) avoidance of additional, unnecessary diagnostic testing; (4) early diagnosis of associated complications through medical monitoring; and (5) reduction of stress caused by diagnostic uncertainty. A specific commitment to identify all patients with CBCDs and obtain their clinical profile and distribution in our country is mandatory; this will help delineate the genetic and phenotypic spectrum of these rare disorders, provide accurate information about prognosis and recurrence risk, and guide further assessment and medical management. In this light, the establishment of an Italian register for CBCDs would represent an extremely useful resource for the assessment, monitoring and prevention of these rare diseases.

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N. 14

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

Hereditary Iron Metabolism Disorders Italian Network

AUTHORS

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ABSTRACT

Genetic disorders of iron metabolism may lead to complications shortening life expectancy or impacting on life quality. Most frequently, they induce systemic iron overload that can be toxic for the liver and many other organs leading to liver cirrhosis, hepatocellular carcinoma, diabetes, cardiomyopathy, hypogonadism, osteoporosis and arthropathy. These forms include the relatively common Hemochromatosis type 1 and the more rare Hemochromatosis type 2 and 3 whose defective genes are involved in the regulation of hepcidin, the master regulator of iron homeostasis. Other rare genetic iron overload diseases are linked to mutations in the ferroportin gene or to rare mutations in transferrin, DMT1 or ceruloplasmin genes, which are also characterized by anemia and/or neurological symptoms. There are also remaining undefined forms of family iron overload. In addition, a rare genetic iron deficiency disorder, named IRIDA, has been recently identified. Diagnosis, characterization and treatment of these heterogeneous forms of genetic iron overload require specialized clinical expertise and extensive genetic studies. However, patients are not equally managed throughout Italy due to the fact that there are only a limited number of expert referral centers. In addition, there is no formal connection between expert centers and peripheral ones, also because of the regional organization of the Italian Health Service. This can lead to delayed or mistaken diagnosis, erroneous utilization and interpretation of the genetic test causing concern for patients and kin and inadequate screening for iron-related complications and therapies. Also, the lack of an established and efficient Italian network for hereditary iron disorders limits: i) epidemiological studies; ii) genotype-phenotype correlations; iii) understanding clinical expressivity and natural history of the disease(s); iv) identification of additional factors involved in yet unexplained forms of iron overload; v) comprehension of the still obscure mechanisms of iron overload and iron-related damage; iv); v) development of new diagnostic, prognostic and therapeutic tools. To overcome these problems, we propose to set up an Italian network made by clinical, genetic, and research units already involved in the management of such patients and in studying mechanisms of diseases, in order to improve patient care, to ensure knowledge improvement and dissemination, and to develop tools for translational research. The units of the network include the Italian centres that are recognised clinical/genetic referral centers and internationally renowned experts in hereditary iron disorders as demonstrated by the relevant number of scientific papers and reviews published to date in prestigious peer-reviewed journals.

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N. 15

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

Initiation of a new rare disease patient registry in Norway, a multi-purpose registry: "to live with a rare disease"

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ABSTRACT

inherited, congenital complex conditions related to the central nervous system. Approximately 3000 users are registered at Frambu covering more than 100 different diagnoses. The approach is multidisciplinary, covering medical, psychosocial, physical and educational aspects, encompassing the whole life span of the person. The overall goal is to promote the best quality of life for persons and families. Frambu is one of ten national Government-funded centers for rare disorders in Norway. Together, these centers cover more than 300 different rare diagnoses. The aim of the current presentation is to present the envisioned registry with an emphasis on challenges and potential benefits. What type of registry is envisioned A non-exhaustive registry designed for research purposes documenting the natural course of disease, taking into account multiple areas such as social interaction and integration, community participation and occupational functioning, and quality of life. To work with groups of diseases with common phenotypic expression with focus on "Living with a rare disease". A longitudinal approach across the age span is planned. We plan to link up to, an already existing rare disease database RAREDIS . We envision a two tier approach with a general section and an special disease specific section. The general part entails a set of common data elements (CDE's) whereas the disease specific registry includes diagnoses categorized after the ICD 10/11 diagnostic code with phenotypic/ genotypic description to classify using ICD and Orphanet classification system/nomenclature. Challenges include (a) determining informants (The carrier of diagnosis, the caregiver, others?) (b) balancing a transdiagnostic general approach versus a disorder-specific approach. (c) inclusion/exclusion criteria (limit to certain diagnoses, age groups, intellectual functioning? (d) how to ensure compatibility / international cooperation, link to other registries, (e) exploring bio-bank possibilities. (f) juridical and ethical issues (e.g., using web based questionnaires, determining consent criteria) The potential advantages in the current setting include (a) a small total population and a "transparent" society with personal id numbers for all inhabitants (i.e. easy to track), (b) a common public health system, (c) possibilities of linking to other national registries, and (d) relative access to funding possibilities Plans and challenges will be presented aiming for a group discussion with input from conference participants. The presentation will be valuable for participants planning or having experience with establishing registries for rare disorders.

N. 16

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

A RARE ADVERSE EVENT INTO A RARE DISEASE. A STUDY FROM THE NATIONAL REGISTRY OF CONGENITAL BLEEDING DISORDERS

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ABSTRACT

Congenital Bleeding disorders are rare diseases, often not immediately identified. The establishment of a specific Registry for these pathologies is recommended by the World Federation of Hemophilia and could represent an important tool in regional and national health organization (1). The National Registry of Congenital Bleeding Disorders (RNCC), realized at the Istituto Superiore di Sanità since 2005, supplies epidemiological data on the prevalence of the different congenital bleeding disorders in Italy, on therapy complications, in particular infections and development of inhibitor antibodies, and on the needs of drugs for treatment therapy (2). Data are collected, with the collaboration of the Italian Federation of Hemophilia Associations (FedEmo) and the Italian Association of Hemophilia Centers (AICE), through a data flow with the 54 Italian Hemophilia Treatment Centers that update their local database and send information to the national database. In 2011 the total number of patients analyzed in the RNCC is 8,411: 43% is represented by Hemophilia A (HA), 9% by Hemophilia B (HB) and 25% by von Willebrand disease, patients with other rare deficiencies are 1,215: 40% of them with Factor VII deficiency. The prevalence/100,000 inhabitants of HA and HB is 5.9 (95% confidence interval: 5.7-6.1) and 1.2 (95% confidence interval: 1.1-1.3), respectively. Severe HA patients (1,690) represent 47% of the total HA patients registered; severe HB patients (273) represent 38% of the total HB patients (2). Actually the development of inhibitor antibodies, especially against Factor VIII, making ineffective the standard substitutive therapy for HA, represents the most relevant adverse event during the therapy. Total patients indicated positive to inhibitor antibodies are 379. Severe HA patients, with clinical history positive to inhibitor antibodies, are 298 corresponding to 18% of the total severe HA patients. Patients, registered with current inhibitor during 2011, are 193, of these 33% registered in the 0-2 year-old group; while the remaining patients are indicated as no more positive to inhibitor. In the presence of FVIII inhibitor antibodies, treatment with a bypassing agent or Immuno-Tolerance Induction (ITI) is utilized (3). Severe HA patients, for which a specific therapy for inhibitor treatment was notified during 2011, are 114: 88% receiving bypassing agents and the remaining part using ITI. The RNCC, monitoring the rare population with bleeding disorders in Italy, is a model of active surveillance that serves predetermined scientific, clinical and policy purposes.

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N. 17

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

Spanish Rare Respiratory Diseases Registries (RRDR): integrated design within National Registry of Rare Diseases (SpainRDR)

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ABSTRACT

We present the general characteristics, objectives and organizational skills of the first 5 Rare Diseases Registries (RDR) integrated within SpainRDR as part of a collaboration deal between Institute of Health Carlos III and Spanish Society of Respiratory Diseases (SEPAR). The diseases collected on these registries are: alpha-1 antitrypsin deficiency (AATD), lymphangioliomomatosis (LAM), pulmonary histiocytosis (PH), alveolar proteinosis (PA), pulmonary sarcoidosis (PS). SpainRDR structure: SpainRDR aims to create a harmonized platform for RDR. Regional health registries, scientific societies and patient organizations are collaborating in this network (see www.spainrdr.isciii.es and <https://registoraras.isciii.es>). Regional health registries collect data from hospital discharge reports and primary care centers, though there are population based. Registries of patients created by researchers and clinical experts shared their information or establish their databases inside SpainRDR platform. They collect clinical outcomes from their own experts populations. Patients association encourage their members to register themselves on SpainRDR website. Development of RRDR: An advisory board formed by clinical experts and supervised by SEPAR scientific committee selected the items and verify the quality of new cases data. Demographical data, tobacco consumption, lung function test parameters, 6 minutes walking test parameters, arterial blood analysis results and quality of life tests were standardized by consensus of participants in order to be comparable for further studies among different diseases. Beside those common variables, each registry included disease-specific items (radiological score, genetic test, occupational exposure...). Databases are available for researchers from several websites belonging to SEPAR and ISCIII. A total of 476 patients are registered on AATD registry. The expected recruitment for 2013 regarding the others is: 70 LAM, 30 PH, 10 PA, 80 PS. Patients collaboration: A total of 91 individuals has registered themselves on SpainRDR website (6 AATD, 7 PH, 60 LAM, 18 PS). It is specially remarkable the role of Patient's association in the successful registry of LAM cases. Conclusion: An integrated platform including information from regional authorities, researchers and clinicians from scientific societies and affected individuals is feasible and useful because it allows to obtained a global view of each disease. Registries of patients obtain very detailed clinical information and follow-up but also they are biased by a restrictive selection of candidates instead of population based registries that included all affected individuals but with a minimum data set. SpainRDR combines both so a more accurate data are available for research and national health programs management.

N. 18

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

The Italian Network for Laminopathies

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ABSTRACT

Laminopathies are a group of genetic diseases caused by mutations in the gene encoding the nuclear protein lamin A/C or in related genes. A group of laminopathies targets specific tissues – tissue-specific laminopathies, mostly affecting skeletal and cardiac muscle or adipose tissue –, other laminopathies affect multiple tissues – systemic laminopathies. The Italian Network for Laminopathies (<http://www.igm.cnr.it/laminopatie/>) is a group of Clinical and Research Centers performing clinical and molecular diagnosis or biomedical research in the field of laminopathies. Aims of the Italian Network for laminopathies are: to connect Italian Centers involved in diagnosis and biomedical research of laminopathies; provide information on the clinical features of Laminopathies to family doctors, specialists and patients; provide the contact information of specialists involved in diagnosis and research on laminopathies; provide updated information on biomedical research in the field of laminopathies; organize an Italian Registry for Laminopathies containing clinical and biological data; establish a bank of biological material; report news on relevant events and meetings; report on funding opportunities in the field of Laminopathies research. The Italian Network for Laminopathies website provides updated information of the Network and of Laminopathies-related events. Interplay between the Italian Association for Myology (AIM), the Italian Association for Progeria (AIProSaB), the Italian Association for Emery-Dreifuss Muscular Dystrophy (AIDMED) national and international associations involved in laminopathy research and the Italian Network for Laminopathies is taking place, with the aim to add value to clinical and research activities.

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N. 19

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

Hospital discharges and mortality registries: two complementary databases for the epidemiological surveillance of motor neuron diseases

AUTHORS

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ABSTRACT

Background/objective: Motor neuron diseases (MND) are characterised by selective degeneration of motor neurons, including the pyramidal fibres in the cerebral cortex, motor neurons in ventral horn cells, and cranial motor neurons. Epidemiological surveillance of this disease will be improved because of the building of a rare disease registry. Selection of valuable data sources is one of the first stages of building a registry. The aim of this study was to evaluate the utility of merging data from a hospital discharge database and the mortality registry to build a registry of motor neuron disease in La Rioja, Spain. Materials and methods: Patients suffering MND in the period 1996-2011 were selected among those registered in the discharge hospital database and in the mortality registry of La Rioja, using the International Classification of Diseases (ICD): ICD-9 codes were 335.2 (excluding 335.23) for hospital discharges and ICD-10 code was G12.2 for mortality. The databases were merged to detect duplicated occurrences and to estimate the number of cases identified by each source. Characteristics of the study population were analyzed: gender, age at discharge, age at death and type of motor neuron disease. Results: Using both databases, 187 MND occurrences were detected. A total of 40 (21.4%) incident cases were only provided by the hospital discharge database; 70 (37.4%), only by the mortality registry; and 77, by both data sources (41.2%). Among the 187 patients, 101 (54.0%) were men and 86 (46.0%), women. Mean age at discharge was 66.2 (64.0 in men and 68.9 in women) and mean age at death was 69.4 (68.1 in men and 70.9 in women). The 88.5% (100/187) of patients registered in the hospital discharge database suffered amyotrophic lateral sclerosis. Types of MND found in the mortality registry cannot be determined since ICD-10 codes do not allow us to distinguish among specific types of MND. Discussion: It remains unclear whether patients detected only by the mortality registry had an out-of-hospital diagnosis of MND or whether diagnosis provided by the mortality register was incorrect. Analysing the accuracy of diagnosis codes in the mortality registry appears necessary to establish that database as data source to build a registry to perform epidemiological surveillance of MND.

N. 20

ABSTRACT TYPE

Poster: *Usefulness of Patient Registries to improve rare disease research*

TITLE

German patient registries for neuromuscular disorders: A brief summary after 5 years of work
Dystrophinopathies (DMD/BMD), Spinal Muscular Atrophy (SMA), Myotonic Dystrophy (DM1/DM2),
FKRPopathies (MDC1C/LGMD2I), Hereditary Neuropathies (CMT) and Myofib

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ABSTRACT

Background Until now, neuromuscular disorders can't be cured or treated sufficiently. New therapeutic options were developed experimentally but are not available yet. First, their safety and efficacy in patients must be proven. The main objectives of the TREAT-NMD registries are to assess feasibility and to facilitate planning of appropriate clinical trials in this field of rare neuromuscular diseases and to support the enrolment of patients in these trials, in compliance with ethical guidelines. Besides, patient registries contribute to essential knowledge on natural history, genotype-phenotype correlations and epidemiology. **Methods** In the framework of the European Network of Excellence (NoE) TREAT-NMD several patient registries for neuromuscular disorders were established in Germany during the last five years. The German cooperating partner is the BMBF-funded Network for Muscular Dystrophies MD-NET. An international harmonised dataset is recorded in these disease-specific national registries and sent to a global database in a pseudonymized way. European legislation and ethical recommendations are strictly followed in this process as specified in the TREAT-NMD registry charter. Decisions are made by an Oversight Committee. **Results** Since 2008, within this cooperation five patient registries were established which are hosted at the Friedrich-Baur-Institute in Munich. These are the German-Austrian registry for Dystrophinopathies (DMD/BMD) and for Spinal Muscular Atrophies (SMA), the global patient registry for FKRPopathies (LGMD2I/MDC1C), the German-Swiss registry for Myotonic Dystrophies (DM1/2) and the German-Austrian registry for Hereditary Neuropathies (CMT). The patients register themselves via online self-report system. Their clinical and genetic data has to be added by their neurologist or neuromuscular specialist in order to receive a high data quality. In total, more than 2.000 patients are registered in these registries whereas the registry for Hereditary Neuropathies will be launched online in June 2013 and the one for Myofibrillar Myopathies (MFM) is still under construction. **Conclusion** The registration numbers are still increasing constantly. Since their establishment the patient registries helped to set up international "standards of care" for DMD and SMA, to use patient's data to plan international multicenter trials and enrol patients into these trails. The registered patients receive a regular feedback on new scientific and therapeutic findings. However, all registries are well accepted by patients and clinicians due to a well-established interdisciplinary contact and regular communication with clinicians, geneticists, patients, patient organizations as well as public and industrial partners. The superior aim is to forward diagnostics and therapeutic options for patients with rare neuromuscular disorders.

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N. 21

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

Inexistent Neurofibromatosis Type 2 (NF2) surveillance in Italy: one national code and one registry for NF1 and NF2, two completely different diseases.

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ABSTRACT

BACKGROUND-Italian Neurofibromatosis Type 2 (NF2) patients are rare and random. They are rare for the low prevalence and they are random for the absence of specific "NF2 clinics", fundamental for follow up and care of this devastating disease. These clinics are well established abroad, i. e France and Great Britain. Moreover they are victims of an Italian jam: a single Italian registry has been established for Neurofibromatosis type1 and Neurofibromatosis type 2, on the basis of the same National code, RBG010 (where G means Group, Decree of the Ministry 279/2001). In reality the two diseases share very few similarities, apart from the name: two different genes on two different chromosomes, 17 for NF1, 22 for NF2, different prevalence 1/3,000 for NF1, 1/30,000 for NF2, different signs, mostly cutaneous and subcutaneous neurofibromas for NF1, schwannomas scattered on central and peripheral nervous system (hallmark of NF2 is bilateral vestibular schwannomas), ependymomas and meningiomas for NF2, different prognosis, more benign for NF1, devastating for NF2, because of complete hearing loss, increased risk of severe disability, impaired quality of life and often death at an early age. Besides the Italian National Registry of Rare Diseases (NRRD) with some data, 14 regional/inter-regional registries are in use, with different organizational structures, objectives, and different data, all absolutely inadequate for identifying NF2 patients. A new Italian NF2 patient organization, "Lega per la Neurofibromatosi 2 ONLUS" has taken on this challenge to get out of this difficult situation. **AIMS**- The aim of our project is to push to create a separate diagnostic code for NF2, to have a web-based registry platform that provides extensive features to ease data collection, organization and evaluation of NF2 patients, to have an Italian network of clinical centres with expertise of NF2 to be harmonized as much as possible with other European Databases and Networks and finally, to push for the the creation of an EuroNF2 as a multistakeholder network. **METHODS**-To collaborate with all Italian regional/interegional centres under the supervision of the Italian National Centre for Rare Diseases of National Institute of Health. To provide support (e.g. Software) to all Centres for the data collection. To have direct patient involvement through a dedicated website that attracts their interest and encourages them to join the registry since many patients go directly abroad for a cure. **CONCLUSIONS**-Our project has just been launched and we report our preliminary results of our ambitious project.

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N. 22

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

Central Registration of core data of patients with rare genetic diseases in Belgium

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ABSTRACT

Remark: multiple abstract topics are applicable Following the recommendations of the European Commission (2009/C 151/02) as well as the Belgian Fund for Rare Diseases and Orphan drugs (2011), the health authorities financed the Belgian Scientific Institute of Public Health to work out the implementation of a central rare disease registry collecting a minimum common dataset. Indeed, as is the case in many other countries, Belgian data on rare disease patients are scarce and fragmented. Primary objectives of the envisioned central registry for rare diseases are epidemiological research such as incidence, prevalence and survival calculations; health-care planning and monitoring; quality of care; facilitation of recruitment of specific patients for clinical trials; to pool core data at the European level to obtain good statistical power and to fulfill administrative roles (e.g. reduce administrative burden associated with reimbursement of orphan drugs). The registry has to follow the recommendations laid out by the Belgian "eHealth Roadmap 2013-2018", for example by using a data-flow compatible with future methods for electronic data-exchange (system-to-system communication using electronic patient records). This ambitious project can only be achieved step-by-step. After careful consideration, several compelling reasons led to the decision to lay the foundation for the central registry by establishing first of all registration of the core data set for patients consulting one of the eight Belgian genetic centres. For the time being, data will be collected in a prospective way. An authorisation request had to be filed with the Privacy Commission explaining in great detail the project. This entailed the following: precisising the target population and the diseases concerned; disease coding used (ORPHA-codes); detailing and justifying the collection of each of the core data (personal and medical ones); data sources and their agreement; obtaining the approval of the eHealth Platform as a trusted third party to use their state of the art eHealth services such as the encoding of the national insurance number to use it as a patient identifier; approval of the dataflow (web service by use of the "eHealthbox"); security measures taken; consent procedures used and exact use of the data for feedback to the centres and reporting to the payers (the NIHDI). The genetic registry as a first horizontal concept will be presented with special attention to the data-flow used.

N. 23

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

The Region of Toscana's Support Center: A counseling and psychology-support call center for oncological and rare diseases

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ABSTRACT

On December the 3rd 2013, the Support Center Rare Diseases came to life in the Region of Toscana, as a further development of the Network Rare Diseases. As a result of this development, and thanks to all the available services, patients can be fully taken care of. The Center's counseling and psychology support service is innovative and has proven to actually help those who find themselves in the condition of dealing with severe diseases. Psychologists and Psychotherapists can be contacted at 800880101 every day, offering information counseling, service orientation and psychological support. In its first eight months, the Center has received 713 requests, coming from patients (50%), patients' families (37%) and Operators (7%). These requests have concerned: information on the available support services (46%); information regarding patients' rights (25%); information on diagnosis and treatment course (16%); psychological support (13%). Those who have contacted us have shown a strong sense of confusion and have manifested feelings of anger towards the National Health Care System, complaining a lack of diagnostic and therapeutic support on its behalf. Some of them were so disappointed in their doctors that they eloped on a sort of "Journey of Hope", wasting physical and psychological energies as well as financial resources. Both patients and their families have shown severe difficulties in accepting and coping with the disease. The Center has proven to be very effective in answering these requests by listening carefully to those who have called, showing them the best course treatment available, comforting them and giving up-to-date and individualized information. Psychological support courses were defined as a way to attend emotional and relational issues, as well as difficulties adjusting to the disease. The support service this Center provides via telephone has made it possible to reach those who for either financial or physical problems have felt lonely and abandoned. It has helped deal with a number of emergencies, thanks to the constant assistance guaranteed. Because of the information it provides and the listening support it offers, it has also helped reduce the sense of confusion and isolation witnessed by many. In conclusion, we believe the Center's Support Service offers a valid solution for many. We believe so also because every single patient is unique, and this requires that his or her treatment be adjusted and personalized, demanding the use of all potential means to reach this goal.

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N. 24

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

Linking the Veneto Region Rare Diseases Registry with Birth Registry and Hospital Discharge Records: a way to estimate the impact of rare diseases at perinatal period

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ABSTRACT

Population-based Registries can be very useful both for health programming and for evaluating the results of policies already taken. The combination of the data coming from Rare Diseases (RD) Registry and Birth Registry (BR) can provide indicators to understand in detail the association between rare diseases and perinatal health. In the Veneto Region, North-east of Italy, about 5 million inhabitants, a web-based RD Registry (monitoring all patients affected by a RD) and a web-based BR (monitoring all birth in the Region) have been established since 2002. Data coming from the merge among Regional RD Register, BR and Hospital Discharge Records (HRD), from 1st January 2007 to 31st December 2011, are presented. In the considered period, 220,915 newborns have been born, 1,008 of them affected by a RD: 4.6 newborns out of 1,000. 75% of newborn with a RD is diagnosed before 5 months after birth. They are affected above all by congenital malformations (45%), metabolic diseases (15%), chromosomal diseases (8%), neurologic diseases (8%), blood diseases (6%) and other (18%) 21.3% of newborn with a RD was born preterm towards 7.4% of the remaining ones and 22.2% weights less than 2,500 grams towards 6.4%. Assisted-reproductive-technology is utilized in 2.9% of pregnancies delivering a newborn with a rare disease comparing to 2.2% of the remaining ones. All prenatal diagnostic invasive techniques (amniocentesis, villocentesis and cordocentesis) are performed more frequently in pregnancies of newborns with a rare disease (28% versus 20%). The distribution of maternal age in newborns with a rare disease is similar to all newborns. In newborns with a rare disease, the prematurity and the low-birth-weight rates are higher than in the remaining newborns. Congenital malformations are the most frequent nosological group. The recourse to prenatal diagnosis is more frequent, even if the distribution of women age is not different. All data deals with a genetic component characterizing familial clusters. The presence of a population-based web-based Register and its ability to integrate with other current source of information (BR and HDR) are of great relevance in giving a correct picture of the ongoing health needs in perinatal population with RD and assessing the effects of likely actions.

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N. 25

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

Lessons learned in updating a large global registry to achieve long-term improvements in data completeness and quality: the Hunter Outcome Survey MOving towards System Enhancement (HOSMOSE) project

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ABSTRACT

The Hunter Outcome Survey (HOS) is a Shire-sponsored, global, longitudinal, observational registry that collects information on the natural history of Hunter syndrome and long-term effectiveness and safety of enzyme replacement therapy with idursulfase (Elaprase®, Shire Rare Diseases). As of March 2013, the registry contained information from more than 900 patients. When HOS was first established in 2005, knowledge of the natural history of Hunter syndrome was in its infancy. As it was not known which variables would be important for long-term analyses of this multisystem progressive disorder, numerous fields covering many different clinical and biochemical assessments were included in the database. The Hunter Outcome Survey MOving towards System Enhancement (HOSMOSE) project was initiated in July 2012 to enhance the data entry process and focus the database towards clinically important parameters. A fundamental element of this ongoing project is to substantially decrease the number of data fields. Key considerations during this process are to establish what information is being collected during routine patient follow-up and ensure that the data collected continue to be clinically and scientifically relevant. Extensive consultation with HOS Investigators and study nurses has been crucial. Updating and improving the HOS platform and user interface is another important component of the HOSMOSE project. The new structure has been designed to better reflect routine clinical practice, ultimately facilitating efficient data entry. The design also aims to optimize the future value of the large amount of information already captured in HOS, and addition of new fields has been minimized. Existing data fields and dropdown lists are being updated to reflect what was previously entered as free text, thus aiding statistical analysis. To increase data quality, more automatic edit checks and guideline text have been included, and improved query functionality within the system will facilitate remote monitoring. Migration of data to the updated platform is being carefully planned and executed, and will be properly documented and validated. Two rounds of user acceptance testing will be performed at appropriate intervals. Finally, extensive quality assessments of the completed system will be performed by Shire and the supporting contract research organization before launch. Data entry by the sites and data extraction will be performed using the original system until the entire process is complete and the new database is thoroughly validated. Internal and site training before launch of the new system will be crucial to its success.

N. 26

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

Approaches to improving data completeness in a global registry in the short term: experience in the Hunter Outcome Survey (HOS)

AUTHORS

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ABSTRACT

The Hunter Outcome Survey (HOS) is a Shire-sponsored, global, longitudinal, observational registry that was established in 2005 to collect information on the natural history of Hunter syndrome and long-term effectiveness and safety of enzyme replacement therapy with idursulfase (Elaprase®, Shire). More than 900 patients are enrolled in HOS (data as of March 2013). A multidisciplinary approach is vital to management of patients with this multisystem, progressive disorder for which numerous clinical and biochemical assessments form an important part of routine follow-up. It can therefore be challenging for HOS sites to collect and enter information from the many different specialists involved. Here, we share our experience in designing and implementing the HOS Data Completeness Project, which aims to improve overall levels of data completeness and quality at a time when registry data are becoming increasingly important in furthering our understanding of long-term treatment effects. Initiated in July 2012, the HOS Data Completeness Project has been developed at the request of and in discussion with the European Medicines Agency. The initiative involves engagement of a third-party contract research organization (CRO) to perform focused data entry at a limited number of HOS sites. Identification of a restricted number of relevant clinical core data variables has been key and has reduced the number of fields to approximately 17% of the total currently available in HOS. The CRO performs data entry both prospectively and retrospectively for these core variables. Provision of appropriate disease area education and practical database training for CRO staff has been crucial. A collaborative approach and frequent communication between Shire and the CRO has facilitated discussion of data entry progress and general observations across the project. Communication with the sites and involvement of local Shire staff from the beginning of the initiative has been vital. Investigators on the HOS Committees, Boards and Working Groups have also received regular updates on project status. Twenty-one sites with a total of 350 patients spread across nine countries and four continents have been targeted for the HOS Data Completeness Project. Activities have already been initiated in six countries, with local data entry support provided in five of these. It is anticipated that the HOS Data Completeness Project will result in a more complete and robust database of relevant clinical data, thus providing insight into long-term treatment effects and also into the true extent of follow-up of patients with Hunter syndrome in real-world clinical practice.

N. 27

ABSTRACT TYPE

Poster: Rare Disease Registries use for public health and health care planning

TITLE

Interregional Network of Piedmont and Aosta Valley for production of masterly extemporaneous compoundings for rare diseases

AUTHORS

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ABSTRACT

Introduction. In 2008 it was set up the Interregional Network of Piedmont and Aosta Valley for prevention, surveillance, diagnosis and therapy of Rare Diseases. With DD n.24 Of 20/01/2010 of the Director of the Health Direction of Piedmont Region it was created a multidisciplinary group for the Prescriptioning of clinical extemporaneous compounding activities directed to patients suffering from rare diseases. The group activities have permitted the punctual fulfillment of what was estimated by the dgr n. 3-13453 of 8/03/2010 concerning the "Experimentation of rare pathologies organization". With DD n. 305 of 10/05/2010 it was moreover approved the "Operative Prescription for production, supply and delivery to patients of masterly extemporaneous compoundings for rare diseases prepared in the regional pharmacies". **Materials and Methods.** The activities undertaken by the group are: mapping of typologies of orphan extemporaneous compoundings for rare diseases usually prepared by the different hospitals; assignation of regional code, ATC code and rate for any extemporaneous compounding to put in file F; elaboration of the Handbook of Extemporaneous compoundings for Rare Diseases; elaboration of the Formulary made up of the preparation schedules for every masterly extemporaneous compounding prepared by the different regional ASL/ASO reporting: composition, preparation formalities, stability and conservation, instruction (in accordance with the doctor), label, literature references; settlement of the regional prescription for the prescription and allocation of the extemporaneous compoundings for rare diseases; determination of the assignment of orphan extemporaneous compounding between the different pharmaceutical services as needed; preparation, in collaboration with the doctors who prescribe, of follow-up schedules in the way to create a system of drug-surveillance, to confirm efficacy and quality data, to obtain helpful material for epidemiological and drug-economic analysis. **Results.** The Handbook and the Formulary of Extemporaneous compoundings for Rare Diseases have been put in the site <http://intranet.ruparpiemonte.it> allowing the consultation by doctors and pharmacists operating in the rare diseases environment, permitting as well the introduction of the extemporaneous compounding therapy in the Official Therapeutical Prescription released through computerized procedure of management of the Regional Register of patient suffering from Rare Diseases. Through the possibility of transfer of orphan extemporaneous compounding preparations for rare diseases between the different pharmaceutical services it was permitted the direct delivery to patients by the respective ASL/ASO. **Conclusions.** An important result has been reached allowing the supply of medicines not available on the market, characterized by high level of quality, efficacy and safety, favouring the welfare continuity.

N. 28

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

From prevalence data to the preterm birth for fetal Gastroschisis- a success story in Saxony-Anhalt, Germany!

AUTHORS

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ABSTRACT

Background/Purpose: An ambitious goal for a population-based birth defects registry is to integrate the clinical expertise with the best available results from epidemiological and clinical research. Gastroschisis is a rare congenital defect of the abdominal wall and has significant morbidity and mortality. More than 20 years ago, when the registry was started, pregnancies affected by gastroschisis were diagnosed at the time of delivery or after fetal death. To date, the majority of cases are diagnosed prenatally. Although the anomaly is repairable with a good potential for a normal outcome the best time of delivery is still controversial. We assess the effects of birth defects surveillance and research (including data from Malformation Monitoring Centre Saxony-Anhalt, Germany) for the management and outcome of fetal gastroschisis in our birth cohort. Methods: We reviewed studies on prevalence, risk factors, perinatal assessment of pregnancies affected by gastroschisis published together with our Partners EUROCAT (European Surveillance of Congenital Anomalies) and ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research) including data from Saxony-Anhalt. We included data from our observational study on 49 gastroschisis affected pregnancies (April 2006 to August 2007) on maternal risk factors, numerous data on pregnancy parameters. Results: Gastroschisis baseline birth prevalence in Saxony-Anhalt is 3.9 per 10,000 births. We will outline trends of live births (LB), stillbirths and fetal deaths from 16 weeks of gestation (FD) and terminations of pregnancy for fetal anomaly (TOPFA) on the prevalence of Gastroschisis in our German birth cohort as well as the influence of prenatal diagnosis on pregnancy outcome and the impact of increasing pregnancy surveillance (Data from 1999 to 2011). Furthermore we will base on the surgical outcome results of 17 patients (2006 to 2012) demonstrate the benefit of a newly established clinical pathway on perinatal management and surgical repair. Babies were delivered by caesarean section between 34-35 weeks of gestation. Assessment of the preterm risk showed no adverse effects of elective preterm birth but benefit for the surgical procedure (All of them underwent a primary closure without any patch. In only 3 cases, enterostoma had to be created.) Conclusion: Overall our preliminary results are able to show benefits of prenatal detection and surveillance of affected pregnancies. Nevertheless clinicians need to balance the perinatal risk of early delivery against the benefits of clinical convenience when making case management decisions after prenatal diagnosis of gastroschisis. But Surveillance data on gastroschisis could help to achieve risk-controlled decisions.

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N. 29

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

High loss of follow-up data from patients included into the Spanish Registry of Patients with alpha-1 antitrypsin deficiency (REDAAT)

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ABSTRACT

Introduction: Severe alpha-1 antitrypsin deficiency (AATD) Pi*ZZ type is a rare hereditary disorder in Spain, with an estimated prevalence of 1: 3,334 individuals, and about of 12.000 carriers of this potentially hazardous deficient genotype, that often predisposes a person to the development of COPD, chronic liver disease, and exceptionally relapsing panniculitis or systemic ANCA+ vasculitis. Nevertheless, one third of them will never show clinical symptoms. The REDAAT collect data from patients affected by severe AATD since 1993 with scientific proposals. The main objective of REDAAT is the knowledge improvement of the natural history of severe AATD, which relies in the systematic collection of follow-up quality monitoring data. Three-hundred and nineteen physicians from all country should register their cases in the REDAAT database (www.redaat.es). Six-months follow-up reports are recommended. The follow-up conclude after transplantation or patient's death. This study analyzes the follow-up failure rate and its possible causes. Results: A total of 467 patients have been included in the Spanish Registry so far. Their distribution by phenotypes is: 359 (77%) Pi*ZZ, 93 (20%) Pi*SZ, and 15 (3%) null and rare variants. The reason that led to a diagnosis of AATD was COPD in 308 (66%) cases; liver cirrhosis in 49 (10%); family screening in 87 (19%) and other causes in 23 (4,9%). The expected follow-up reports for this population were 951. A total of 630 (66%) follow-up reports were recorded. A 11,2% of non reported follow-up were expected because of transplantation, death registered on the previous one follow-up or less than 6 months from the previous one. Conclusion: We observed a high rate of follow-up failure which do not appear to be justified by objective and serious reasons, such as transplantation or death. This remarkable loss of follow-up data decreases the total number of available cases for a natural history comprehensive analysis. Encouraging actions to promote the follow-up reports among the REDAAT collaborators to maintain and update the initial enrollment information are required.

N. 30

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

Improving quality of European Cystic Fibrosis Society Patient Registry Data

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ABSTRACT

The European Cystic Fibrosis Society Patient Registry (ECFSPR) collects data from national registries and individual CF centres from pan-European countries since 2003; it includes demographic and clinical data of more than 26,000 patients from 23 countries. According to the ECFSPR data quality assurance procedure, the software developed for the ECFSPR automatically performs checks for out of range values and, after data collection completion, the statistician performs internal coherence controls and the national registries and the CF centres have to correct or confirm the values detected as incorrect. In the first years of the set up of the ECFSPR, the national registries representatives suggested improvements on the data quality assurance procedure. They perform their quality controls on the national data and freeze the databases a few years before the ECFSPR data collection (ECFSPR collects data with a delay of three years). Moreover, to address the correction requests, the need to contact the individual centres in their country makes this a very long and inefficient process especially for big registries. In order to standardize the quality controls and optimize the efficiency of the process, a data quality control group was organised with the aim to establish a complete list of data quality controls to be performed on all national databases before the uploading. The working group, composed of national registries data managers and the ECFSPR team, collected the list of controls from the different national registries and, starting from the ECFSPR list of data quality controls, drafted a shared list that was discussed and modified mainly with a web-based tool for sharing documents and for discussions. The experience and the expertise of each member of the working group allowed creating a complete and shared list of data quality controls that will be performed by all national registry data managers before the uploading on the ECFSPR server: in this way the data uploaded will be already cleaned according to the ECFSPR data quality controls and the amount of requests of corrections and confirmation will be reduced or null. The next step will be implementing the data quality controls on the software and uploading data from selected national registries as a pilot. Completeness of the data, check of the inclusion criteria and concordance between the source of the data and the collected data are other crucial issues for the ECFSPR: these could be the next challenges for the data quality group.

N. 31

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

An empirical investigation of Primary Care Health Professionals Attitudes towards Rare Diseases

AUTHORS

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ABSTRACT

Aim of the research was to assess the views of health professionals on the social aspects of treating patients involving the testing priority and the right to medical treatment and acceptability of the higher treatment costs of patients suffering from rare diseases compared to common diseases. Method: The prospective cross-sectional study was conducted in the second part of the 2012 year and first half of the 2013 year, using specially created questionnaire on a convenient sample of health professionals on the primary level of health care system in Serbia. The self-assessment of attitudes and awareness regarding the importance of public health of rare diseases as well as the availability of appropriate drug therapy and incentives in the research and development of drugs was estimated with five points on the Likert scale graded from "not at all disagree" to "strongly agree". Results: In all, 524 health professionals were surveyed; 79.8% of whom were pharmacists and 20.2% physicians, and they were mostly females (93.50 %). Approximately two-thirds of participants (68.5%) fully agreed with the equitable distribution of health resources to achieve that greatest benefits for health (56.4%) and that RDs patients might have the right to reimbursement of ODs even though the therapy was very expensive (62.6 %). Only 40.9% of participants completely agree with the attitude on healthcare budget allocation for RDs patients, even when there was no evidence that maximum health improvements could be reached. Almost half of the respondents (46.7%) think there is a lack of public awareness in the society regarding the rare diseases. T test for independent samples showed that there was no significant difference in attitudes among pharmacists (M = 4.13 SD = 2.70) and physicians (M = 4.20, SD = 0.92), $t(512) = 1.375$, $p = 0.11$. Conclusion: Among the Serbian health professionals is expressed the social priority of equal rights for treatment of patients with rare diseases and those with common diseases. There is also readiness to support a greater commitment of funds intended for patients with rare diseases, which may justify the special status of funding the drugs for rare diseases. Project of the Ministry of Science and Technological Development of the Republic of Serbia, No 41004 and 175036.

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N. 32

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

The increase of Rare Disease in rural areas. Which can be the contribution of sickle cell disease and Thalassemia Specialist Nurses in the registering of new case?

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ABSTRACT

Background: Over 300 000 babies with severe haemoglobin disorders are born each year. Approximately 5% of the world's population carries trait genes for haemoglobin disorders, mainly, sickle-cell disease (SCD) and Thalassemia (Thal). Some regions like South East Asia, Mediterranean basin, and the Middle East, Beta- Thal is common. In Africa (Nigeria) SCD is predominate; in some area there are conditions that the gene prevalent is up to 25 %; however population migration has spread these diseases to most countries. There are not exactly data for rural area population in some large under developing country. Methods: The health burden of haemoglobin disorders can be effectively reduced through management and prevention programmes. In advanced countries, like UK and US there are demonstrations that specialist nurses with public health competency, applying primordial and primary prevention reduce the percentage of SCD and Thal patient, using less budget. The specialist nurses can operate also in underdeveloped health care systems, rural areas by starting up small centres composed from 2 nurses, 1 e- haematologist consuler and national electronic register. Using a low cost budget and collaborating with local administration increase the success of this project. Results: Increase awareness of the international community of the global burden of these disorders; Promote equitable access to health services; promote and support research to improve quality of life for those affected. Conclusion: In developing countries, the specialist Nurses can have a key role in the prevention and registering of rare genetic disorders diseases by using their entire scientific competency and providing technical support to countries.

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N. 33

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

Rare disease registries – a policy decision-making tool for better access to orphan therapies

AUTHORS

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ABSTRACT

Rare disease policies have the ultimate objective to provide better treatment and care to rare disease patients. Patients do want to see increased life expectancy and better quality of life. Orphan medicinal therapies are designed and promoted to comply with these expectations. The orphan legislation has ensured enormous material and human resources for discovering new therapies for orphan drugs. Nevertheless, more than a decade after the launch of EU rare disease policies, a considerable amount of the marketed orphan medicinal products are not accessible in the majority of the Member States. Rare disease patient registries represent an efficient tool to assess orphan drugs' added value and to provide policy makers with a legitimate base for decision-making. Our review study examines the relation between specific national rare disease registry initiatives in the EU and the process of health technology assessment of orphan drugs and their subsequent reimbursement by public funds. Patient registries allow improving access to orphan therapies by developing evidence of safety, clinical effectiveness and patient impact. This enables health authorities to prioritize national plans and model future costs to better understand funding ramifications and create sustainable reimbursement platforms.

REFERENCES

rare diseases, orphan drugs, decision making.

ABSTRACT TYPE

Poster: *Rare Disease Registries use for public health and health care planning*

TITLE

Evaluation of Cost of Illness (COI) and Health Care Burden in Duchenne Muscular Dystrophy

AUTHORS

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ABSTRACT

Background Duchenne Muscular Dystrophy (DMD) is a fatal inherited neuromuscular disorder which affects one in 3.600-6.000 live male births. Affecting cardiac and skeletal muscle it results in muscle weakness and atrophy in young children leading to wheelchair dependence in their teens and dramatically reduced life expectancy of 25 to approx. 35 years due to cardiac and pulmonary failure. Due to progressive disablement this disease results in reduced working capacity and high health care utilization not only by patients but by their caring relatives. Until now, there is no cure for DMD. New promising therapies like exon skipping are emerging and have reached clinical developmental status. **Objective** Clinical development of these promising therapies is costly and once approved by regulatory authorities implementation in DMD care may produce high expenditures for the health care system. Despite their own cost, the potential contribution of innovative therapies could also reduce the cost of illness (COI) under standard care. In order to forecast the balance from a health economic perspective, our study aimed at assessing the current cost of illness as a first step. **Patients and Methods** In order to determine the COI, a micro-costing method was used to examine the direct and indirect costs measuring the economic burden of DMD on patients, relatives and society. Corresponding questionnaires were sent to patients using an established German DMD patient registry. Personal interviews were performed with the selected target group including patients and their relatives. By using cost of illness analysis the data were analyzed. **Results** In total, questionnaires were sent to 560 patients. The age of the patients ranged from 1 to 40 years. In the light of current standard DMD care the economic burden of patients, relatives and their families were compiled and analyzed. Relevant socio-political implications have been identified and compiled. **Conclusion** Our results provide for a thorough cost of illness analysis (COI) which represents the first step towards a systematic health economic assessment of innovative DMD therapies. The results will be used in further planned evaluations such as a cost utility analysis. Particularly, as a thorough preparation of the health economic implications is required, the study results enable to speed up preparation of payer discussions and negotiations with regard to pricing and reimbursement. In this context our results contribute to the facilitation of a smooth translation of innovative DMD therapies from their discovery to their implementation into DMD standard care.

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N. 35

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Exome sequencing as diagnostic tool for rare diseases

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ABSTRACT

The identification of a causative mutation for a rare (Mendelian) disease enables molecular diagnosis and carrier testing in the patient and his or her family. It also serves frequently as a starting point for therapeutic interventions. Over the past couple of years this topic received a boost by the introduction of 'next generation sequencing' (NGS). There are two unbiased sequencing approaches available, whole genome sequencing (WGS) and whole exome sequencing (WES) respectively. At present the latter, studying only the 1% of the genome comprising the protein-coding (exome) part of our genome, seems ready to be translated into clinical practice. Based on recommendations developed by our group within of the DG SANCO project EPIRARE, within the recently started EC DG Research project "RareBestpractices", we will use exome sequencing as a case for the 'horizon scanning' part in WP4 to: 1. Monitor the emerging evidence from basic science (genomics) to identify future research and policy needs of WES. 2. Use the innovative LAL model as an overarching translational pipeline from basic sciences to healthcare systems combining technology transfer tools (TT) and policy-making tools. At present, a variety of successes have been documented both in the scientific and popular domain, including Nick's story, Retta's Beery's non-identical twin story and most recently Bea's project. These promising results already initiated large scale initiatives in the US like the establishment of three Centers of Mendelian Genomics. From a European prospective it will be a challenge to integrate Dutch efforts into other initiatives like RD-connect, EURENomics, NeurOmics and the European Genome-Phenome Archive (EGA), hosted by EBI. The project RareBespractices can play a key role in identifying best practices for translational research in the area of rare diseases taking into account the results and recommendations developed by these European initiatives. Finally, how this new diagnostic tool of exome sequencing, including the data generated, will be implemented in specific European Member States is a topic of ongoing discussions such as being the case currently in the Netherlands. Here, it will probably be addressed in the forthcoming National Action Plan on Rare Diseases that will be presented to our Minister of Public Health by the end of this year.

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N. 36

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

SIX NOVEL MUTATIONS IDENTIFIED IN SEVEN NEW CASES OF NONKETOTIC HYPERGLYCINEMIA, INCLUDING A LARGE DELETION OF GLDC GENE

AUTHORS

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ABSTRACT

BACKGROUND Nonketotic hyperglycinemia (NKH) is an inborn error of the glycine metabolism, caused by the deficiency of the glycine cleavage system (GCS), transmitted as an autosomal recessive disorder and resulted in high levels of glycine in all tissues including the brain. The GCS complex consists of four components: P, H, T and L-proteins, encoded by GLDC, GCSH, AMT and GCSL genes. Approximately 70%–75% of NKH patients are found to have GLDC mutations, with AMT mutations accounting for most of the remaining cases¹. **METHODS & RESULTS** Since 2010 we analyzed 7 cases of neonatal NKH, all from Southern Italy, except two infants, born in North Italy. All patients have elevated glycine concentrations in amino acid analysis of cerebrospinal fluid and/or plasma. Molecular analysis was performed by PCR and sequencing of the complete coding sequence of the GLDC, AMT and GCSH genes. In three compound heterozygous patients we identified 6 mutations in AMT or GLDC genes, 4 of which were novel. Their pathogenetic role has also been confirmed by bioinformatic predictions. Other two patients, one of Moroccan origin, born to consanguineous parents, and the second of Colombian origin, were homozygous for two novel mutations: a large deletion, including exons 1-15 of GLDC gene, and a nonsense mutation, in exon 1 of AMT gene, respectively. Deletion was confirmed by array-CGH and breakpoints were well defined by targeted PCR. All mutations found in probands were detected, at heterozygous state, in own parents. Lastly, two patients were negative to mutation screening by sequencing and array-CGH and are going to be also analysed by MLPA analysis of GLDC gene. Furthermore, in three years we carried out three NKH prenatal diagnoses in two families, whose probands were previously analysed at foreign centres. Molecular prenatal diagnosis performed in our centre, identified one healthy, one carrier and one NKH affected foetus. Pre- and post-analysis genetic counseling has been offered in all cases of both post-natal and pre-natal diagnosis, as it is integral in providing ongoing support for patients and their families. **CONCLUSIONS** To our knowledge we are the only Italian laboratory to run the molecular diagnosis of NKH, thus allowing final diagnosis, particularly necessary when biochemical tests are borderline, for carriers detections and prenatal diagnosis.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

HOMOCYSTEINE REMETHYLATION DEFECT DUE TO TWO CASE OF SEVERE METHYLENETETRAHYDROFOLATE REDUCTASE DEFICIENCY

AUTHORS

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ABSTRACT

Deficiency of enzymes 5,10-methylenetetrahydrofolate reductase (MTHFR), methionine synthase reductase (CblE) and methionine synthase (CblG), and homocysteine CblD-variant-1 are primary homocysteine remethylation defects, characterized by an isolated defect in methionine synthesis without methylmalonic aciduria¹. Among these defects the most common one is MTHFR deficiency, rare autosomal recessive disorder with severe hyperhomocysteinemia, homocystinuria and hypomethioninemia. Patients show a range of neurological and vascular complications, including developmental delay, mental retardation, seizures, motor and gait abnormalities, and thrombosis². In this study, we analyze two patients, first cousins, who presented neurological symptoms of variable severity, suspected for homocysteine remethylation defects, as in both patients metabolic screening have showed plasma accumulation of total homocysteine (>130 µM; reference value 5-15 µM), low plasma methionine (<10 µM; reference value 15-30 µM), no urinary methylmalonic aciduria excretion and normal serum vitamin B12 and folate levels. In our patients, therapy with folinic acid and betaine was started as soon the clinical suspect arose but they improved clinically and biochemically slightly. We firstly performed molecular analysis of MTHFR gene, using 12 specific primers for amplification of genomic DNA by PCR and for direct sequence analysis of coding regions. Both patients resulted compound heterozygous for 2 mutations in the MTHFR gene: c.547C>T (p.R183X) in exon 4 and c.1013T>C (p.M338T) in exon 6, both previously described as being associated with MTHFR deficiency. In addition, polymorphisms c.665C>T (p.A222V), known as genetic risk factor for vascular disease, and c.1305C>T (p.P435P), associated with preeclampsia, were present in both patients. In conclusion, genetic test for MTHFR deficiency ensures differential diagnosis among homocysteine remethylation defects. Moreover, co-existence of two mutations very harmful (a nonsense mutation and missense mutation, already showed with very low residual enzymatic activity, further reduced by the presence of the polymorphism p. A222V 3) probably justified the treatment failure using folinic acid and betaine.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Epidemiologic survey of a restricted area in Southern Lazio for Spinal and bulbar muscular atrophy (SBMA)

AUTHORS

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ABSTRACT

Introduction Spinal and Bulbar muscular atrophy (SBMA) is an adult-onset, X-linked recessive trinucleotide, polyglutamine disorder, caused by expansion of a polymorphic CAG tandem-repeat in exon 1 of the androgen-receptor (AR) gene on chromosome Xq11-12. Bulbar and spinal muscular atrophy was first described in 1968 by Kennedy et al. The genetic defect was discovered by LaSpada et al. in 1991. The strong negative correlation between the size of the CAG-repeats and onset of the clinical manifestations was first documented by Igarashi et al. in 1992. Although relatively frequent only a few large families have been reported allowing for intrafamilial variability assessment. **Aim** To describe a large series of patients originating from the same restricted area of Southern Lazio. **Materials and methods** Over the last few years several consecutive men have been referred to our center for evaluation and were diagnosed as affected by SBMA on clinical grounds and subsequently confirmed through genetic analyses. Upon closer inspection four of them were born in the same small city of Ferentino (20.000 inhabitants) in the province of Frosinone South-East Lazio. This prompted us to look for additional patients through family investigation and direct interviews with local practitioners. We tried to trace back the deeper family relationships to identify common affected male or carrier female ancestors. **Results** Six additional patients have been identified both living in Ferentino and elsewhere in nearby regions. Most of them had received a clinical and genetic diagnosis at other clinical centers but were relatively unaware of the high prevalence of the disease in the same area. Surprisingly, upon detailed reconstruction of the family trees through direct interviews, no clear recent shared relationship among the patients could be ascertained, with the exception of a couple of brothers and a couple of maternally related cousins. The patients were aged 46-77 years, the CAG expansion is in the typical range for the disease (disease associated repeats 38-62; normal values 10-36); their clinical status ranged from mild initial to severe late disability with 2 wheelchair-bound patients. **Conclusions** Our study identified a cohort of patients with SBMA originating from the same restricted area, likely representing the largest series so far described in Italy and elsewhere (Lund et al, 2000; Karaer et al, 2010). Such an extended series of patients provides the ideal background for detailed assessment of genotype-phenotype correlations and intrafamilial variability. The lack of obvious direct family relationships points to a deep shared ancestry through a series of generations of female asymptomatic carriers. On the other hand a large number of carriers is anticipated raising the problem of extensive search in the area with the purpose of ad-hoc genetic counseling.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Spinocerebellar ataxia type 10 in a peruvian woman in Italy

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ABSTRACT

Objectives: Spinocerebellar ataxia type 10 (SCA10) is an autosomal dominant neurodegenerative disorder manifested by ataxia and seizures, caused by a large expansion of an intronic ATTCT pentanucleotide repeat in the ATXN10 gene on 22q13.3. Normal alleles have from 10 to 29 repetitions while affected people's alleles have up to 4500 repetitions [1]. Herein we report on the first patient with SCA10 in Italy. Materials: A 45-year-old woman from Lima (Peru), living in Italy since, had started complaining at age 35 of slowly progressive unstable gait, dysarthria and dysphagia. Family history was apparently unremarkable. On clinical examination she presented mild dysarthria, unsteady and broad-based gait needing for occasional support, upright posture oscillations, lateral nystagmus and fragmentation of slow gaze movements, hypotonia, adiadochokinesia and poor segmental limb coordination prevalent in her upper limbs. Brain MRI revealed mild atrophy of cerebellar vermis. Screening for anti-cerebellar, anti-GAD 65, anti-gliadin autoantibodies and genetic tests for SCA1, SCA2, SCA3 all gave negative results. During hospitalization she experienced an episode of transient loss of consciousness. Upon deeper enquiry she reported frequent similar episodes since a few years. An EEG showed diffuse epileptiform discharges with occipital and temporal prevalence. Antiepileptic therapy with Levetiracetam (500 mgs b.i.d) was followed by prompt clinic response and EEG normalization. Results: Prompted by the unusual association of cerebellar ataxia and epilepsy and her South American origin we decided to perform genetic investigation for SCA 10 which identified a pathologic expansion (> 280) of ATTCT pentanucleotide in the ATXN10 gene. Discussion: SCA 10 is the second most frequent genetic ataxia in Brazilian and Mexican families. It has recently been shown to have a more widespread occurrence in other Latin American countries, but not in Peru so far, in patients with Amerindian ancestry (2). Conclusions: Even though SCA10 has never been reported outside Latin America and East Asia it should be considered in patients living in Europe with suitable genetic background. The clinical phenotype is usually characteristic, but the occurrence of absence seizures can be overlooked by patients and their families and should be carefully investigated.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Analysis of carriers of Friedreich Ataxia: prevalence and practical implications

AUTHORS

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ABSTRACT

Objectives: Friedreich's ataxia (FRDA) is the most common of the hereditary ataxias. It is an autosomal recessive neurodegenerative disease (1), with a prevalence of approximately 2×10^{-5} in Caucasian populations. The majority of FRDA patients are homozygous for an unstable GAA trinucleotide repeat expansion in the first intron of the frataxin (FXN) gene on chromosome 9q13. Normal chromosomes have 8-33 GAA repeats while FRDA chromosomes have 67-1300 GAA repeats. Detection of the expansion mutation provides a very useful diagnostic test. Carrier frequency has been deduced from the prevalence of the disease and is estimated to be 1 in 90 (2). Clusters due to a founder effect have been reported in Rimouski, Quebec and Paphos, Cyprus (3). Carrier status determination in relatives of FRDA patients and their spouses is not firmly established as part of clinical management so far. We report on our practical experience in the field. **Materials:** We decided to review our series of FRDA patients to gather information on the determination of carrier status and draw practical considerations. **Methods:** Genetic diagnosis and carrier status have been performed according to current criteria for genetic testing in FRDA (1). **Results:** We reviewed clinical information regarding 47 patients (3 deceased) from 37 families. In 8 families multiple cases occurred. 30 patients are residents of the Lazio region with an estimated population of 5.626.000 (2008). We identified 8 patients among immigrants, notably 6 Albanian patients. Only in 3 out of 37 families known parent consanguinity was reported. We identified 101 carriers, 75 parents, 9 children and 43 sibs of FRDA patients. We tested also for carrier status 27 spouses of previously identified carriers (usually because they were relatives of FRDA patients). Surprisingly we identified 2 non related individuals which tested positive. Prenatal diagnosis was requested in both cases. Moreover we encountered a very unusual instance of a male carrier who had two affected children from two unrelated carrier women. **Discussion:** Carrier frequency might be underestimated. This could explain the high occurrence of FRDA patients from apparently non consanguineous parents or other unexpected observations. **Conclusions:** We suggest that carrier status determination should be considered as part of clinical management of FRDA patients. Better communication about such a sensitive issue should be encouraged with families of FRDA patients and public resources allocated for this purpose.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Chiari Syndrome and Syringomyelia Registry: advances in natural history, epidemiology and clinical phenotypes from a North Western Italy cohort.

AUTHORS

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ABSTRACT

Background: In Italy and in Europe Chiari Syndrome (CS) and Syringomyelia (Syr) are classified as rare disease (RD), but currently known occurrence data in EU are missing. The increased ability to diagnose Chiari Malformation (CMI) and Syr by MRI and its widespread availability has led to an increase of reported cases, often asymptomatic, with the need to standardize definitions, diagnostic criteria and treatments. Aims: we propose shared Interregional Recommendations with the primary aim to estimate prevalence and incidence of Syr and CMI in Northern West Italy, with special reference to their clinical correlates (symptomatic forms); a further aim is to regulate the patient access to exemption path for RDs, according to Italian Law. Methods: standardization of diagnostic criteria (clinical and neuroradiological) and surgical Recommendations by the multidisciplinary and interregional Piemonte and Valle d'Aosta Chiari-Syringomyelia Consortium (CSC); census of Syr and CM patients by a dedicated census form developed by CSC and shared with every specialists involved in diagnosis. The following data were extracted: socio-demographics, age at diagnosis, age at survey, diagnostic delay, MRI parameters, diagnosis, associated conditions, neurological symptoms/signes, types of surgery. The prevalence (=number of Syr and CS diagnosis at 2011) and the incidence (=number of new reported cases in 2011) for symptomatic forms were estimated using both Interregional Piemonte and Valle d'Aosta RD Register and CSC census data, instead for asymptomatic forms was exclusively used the CSC census data. To calculate the relative prevalence and incidence rate for Piemonte and Valle d'Aosta population was considered who were alive in 2010 according to 2012 ISTAT data [1]. Results: 434 patients, 291 females (67%), met diagnostic criteria for Syr and/or Chiari Malformation. Demographics, MRI parameters, diagnosis, prevalence and incidence are reported respectively in 217 Syr and in 347 CM patients. Major neurological symptoms in CS and in Syr respectively are: headache (48%; 28%), cervical pain (30%; 24%), loss of balance (30%; 18%); major neurological signes (sensory-motor, cranial nerves, neuropathic pain, dysautonomic), familiar and clinical history are analysed. Conclusions: first Italian epidemiological data on Chiari Malformation and syringomyelia were achieved, including estimated prevalence and incidence for symptomatic and asymptomatic forms, according to diagnostic CSC Recommendations. Future perspectives: adoption of CSC Recommendations at National level to standardize access to diagnosis and care process; dissemination of census in the National context; promotion of clinical trials, i.e. multi-center prospective study to evaluate surgery efficacy in different clinical forms (CM1 with or without Syr).

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

DEVELOPMENT AND OPTIMIZATION OF A TOPICAL EMULSION FOR THE TREATMENT OF ICHTHYOSIS

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ABSTRACT

Introduction: The aim of this work was the design of a new galenic cream for ichthyosis patients. Ichthyosis is a rare disease for which it is necessary the daily applications of formulations with emollient and moisturizing agents to alternate the use of the power keratinising. These preparations on the market are registered as medical devices. **Materials and Methods:** In collaboration with the Department of Drug Science & Technology, at the laboratory of Pharmacy St. John Baptist, a series of water in oil emulsions were developed. Their qualitative composition is described below. Oil phase: mineral oil, white soft paraffin, palmitic acid Emulsifier: Arlachel 83 Aqueous phase: glycerol, chitosan LW, urea, Kemipur 100, distilled water Three different concentrations of palmitic acid were evaluated. The oil phase, containing the emulsifier, is heated, and then mixed with the aqueous phase using a turbo mixer. The emulsion was characterized measuring the pH and the change in viscosity over time, using a pH meter and a rotational viscometer. **Results:** These formulations, forming a film on the epidermal surface, thanks to the external oil phase, remain on the skin for long time, reducing the transepidermal water loss, allowing lasting hydration. These formulations were stable and their viscosity suitable to act as moisturizing and softening affected skins. The composition of the final formulation identified as the most appropriate is described below. Phase oily (25-27%): vaseline oil 15%, viscous vaseline 10%, palmitic acid 0,5%-1%-2% Emulsifier (10%): Arlachel 83 10% aqueous phase (65%): glycerol 5%, chitosan LW 0.7% to 5%, urea 5%, Kemipur 100 0.1%, MilliQ water qb 100%. The pH of the emulsion is about 5.5 and is stable over time for at least a month. **Conclusions:** The clinical need focused on the study of a new topical formulation for the treatment of ichthyosis, which allows available alternative to current treatments on the market that appear to be less specific to the disease and expensive for patients. In this work it was possible to realize a new preparation, which will be prepared in the hospital pharmacy according to the demands of the center prescriber, as part of interregional network of rare diseases.

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Mitochondrial mutation in adult patient with Hypertrophic Cardiomyopathy and renal failure

AUTHORS

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ABSTRACT

Background: Mitochondrial diseases (MDs) (1:5000-10000) represents a wide group of human disorders associated with mitochondrial DNA (mtDNA) variations causing defect of oxidative phosphorylation system, whereas nuclear genome mutations are somewhat rare. The extremely heterogeneous clinical phenotype, extending from oligosymptomatic condition to complex syndromes involving neurological, ophthalmological, gastroenterological and endocrine features, depends to the involved tissue well as to the specific mtDNA mutations and their heteroplasmic level. Diabetes and deafness are common features of mitochondrial diseases, while renal alterations are rarely reported, especially in adults, probably because of lack of association to mitochondrial conventional phenotypes. Case Presentation: We investigated a 62 years old male affected by hypertrophic cardiomyopathy (HCM) and renal failure that caused already a bilateral transplantation. Pathological anamnesis revealed also diabetes, deafness and Crohn disease. Family history of cardiomyopathy showed a strong mitochondrial involvement. The proband's mother, three brothers (one of which died of renal failure at 26 years), the sister and her child were affected. Materials and Methods: Genomic DNA from peripheral blood and buccal cells was extracted with the Kit-Nucleon-BACC2 (Illustra DNA-Extraction Kit-BACC2-GE Healthcare, UK) and the whole mitochondrial genome was amplified by two pair of primers designed in our laboratory to generate two overlapping fragments. The PCR products were then sequenced and compared to mitochondrial reference sequence (rCRS NC_012920). Results and Discussion: In both biological samples the mtDNA analysis showed the heteroplasmic A3243G mutation in the tRNA^{Leu} (UUR), frequently associated with MDs. A cardiological involvement leading to hypertrophic remodelling, caused to mitochondria intermyofibrillar proliferation, occurs up to 40% of patients with mtDNA disease. Molecular backgrounds of mitochondrial cardiomyopathy of adult age are still quite poorly known and the A3243G mutation in tRNA^{Leu}(UUR) of mtDNA has been reported in 40-60% of patients with HCM. The interesting finding presented here support the knowledge that mitochondrial gene alteration represents a possible etiology in cardiological patients with unexplained renal failure. This is particularly true, as in this case, when other associated symptoms linked with dysfunctional oxidative phosphorylation are present. The case presented in this report further suggests that a differential diagnosis in presence of HCM should be solved by a multidisciplinary approach together with mutation analysis of mitochondrial DNA. Keywords: Hypertrophic Cardiomyopathy, Mitochondrial Diseases, Renal failure.

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3. Schon E.A., Di Mauro S., Hirano M. Human mitochondrial DNA: roles of inherited and somatic mutations. *Nature review*, 2012, 13;878-890

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

"The effect on the quality of life in children with rare diseases"

AUTHORS

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ABSTRACT

Introduction Disability is defined as the consequence or result of a complex relationship between the state of health of an individual and personal, environmental factors representing the circumstances in which he lives. The presence of children with disabilities, specifically with rare diseases, can affect the quality of their lives. Our study aims to evaluate the correlation between the specific factors of the disease and the primary relationships. **Method** The sample consists of 32 subjects with an average age of 9.7 years \pm 4 years. The subjects present motor, cognitive and visual impairments: 71.9% have all three impairments, 21.9% have visual and intellectual impairments, and only 6.3% have a visual impairment. In this sample, 11 individuals have rare diseases and 14 have severe prematurity. The study has involved the use of the ICF classification as a research tool for measuring outcomes and the quality of life. In order to deepen the relationships between the severity of the disease and the quality of family life, the team has focused its attention on three ICF classification codes: D760, E310, E340. The team, consisting of a Child Neuropsychiatrist, Psychologists - Psychotherapists and Professional Educators, has used videorecordings. **Results** The resulting data relating to particular interpersonal relationships, code D760, show that 7 out of 32 subjects have a complete difficulty in creating and maintaining family relationships. The primary relationships between the family and the child are socially and contextually inadequate in the implementation of the actions and tasks required for simple and complex interactions. In relation to code E310, a meaningful positive value has come out, since, on average, immediate families act as a facilitator to the child in situations in which they must provide concrete physical and emotional support. Furthermore, the individual attitudes of immediate family members with respect to social, political and economic beliefs, code E410, are a barrier for the wellbeing of the most families involved in the study. **Conclusion** An early identification of dysfunctional systems child-parent and the interventions aimed at reducing stress have the potential to decrease the frequency and intensity of children emotional and behavioral disorders. In particular, when an early clear diagnosis has not carried out, particularly occurring in rare diseases, an impairment of intrafamilial relationships comes out. This also affects the performing requirements that parents ask the children and invalidate the execution of their actions and tasks. **Key words** Impairments – rare diseases – ICF – family – facilitator - barrier.

ABSTRACT TYPEPoster: *Case-Studies***TITLE**

Molecular diagnosis and clinical characterization in hypotonic Mexican patients. The joint venture experience between the Centro Médico Nacional de Occidente (CMNO-IMSS) and Asociación Mexicana de Atrofia Muscular Espinal (AMAME)

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ABSTRACT

Spinal muscular atrophy (SMA) is a disease with an autosomic recessive inheritance, characterized by a degeneration of the moto-neurons of the spinal cord. Causing a progressive muscular weakness leading to hypotonia. SMA is now a day the main cause death in genetic diseases under two years old (nosocomial infections and respiratory insufficiency). SMA is classified in four types depending on the severity of the disease (0,I,II,III and IV). The molecular techniques are the gold standard for diagnosing SMA; most frequent mutation is the deletion of the 7th exon of the SMN1 gene. The differential diagnosis of SMA many trials and test have to be done since many diseases course with hypotonia like glycogen storage disease type II (POMPE), and other central nervous diseases. Molecular diagnosis approved by the FDA is the endpoint PCR, and the enzyme digestion. In our laboratory, allele specific PCR performed on a real-time platform is used. According to the TREAT-NMD (www.treat-nmd.eu) the gold standard technique for the diagnosis is MLPA (Multiplex Ligation Dependent Probe Amplification), since it can establish the extension of the deletion of the SMN 1 gene, detect mutations that are not in the 7 exon of the SMN1 and other genes. Objectives: The aim of the present work was to: Evaluate the relationship between PCRSA-RT and MLPA, to know which is the most effective assay for SMA, Use the PCRSA-RT to detect the 7 exon deletion of SMN1 gene of 54 hypotonic Mexican patients with a clinical diagnosis of SMA that were send to the CMNO-IMSS and to the AMAME (Asociación Mexicana de Atrofia Muscular Espinal) from the mexican states of: Jalisco, Veracruz, Tepic, Michoacán, Aguascalientes, Chiapas and Mexico City; Establish the percentage of correlation between the PCRSA-RT and MLPA, on the detection of the deletion of the 7 exon of SMN1 gene, and to Describe the phenotype of the patients that have a deletion of the 7 exon of the SMN1 gene. Methodology and Conclusions: Of 27 patients positive for the deletion of the 7 exon of the SMN1 gene done by PCRSA-RT, 15 of them were correlated with MLPA having this a 100% correlation between both techniques. Of the patients that were screened with the MLPA technique, 93% of them have the deletion of the 7 and 8 exon of the SMN1 gene. One of the patients screened with the MLPA technique had 4 copies of the SMN2 gen and another patient had 3 copies of SMN2 gene. Therefore mentioned patients did not have a correlation between the clinical phenotypes and the amount of copies of the SMN2 gene. Based on the phenotype of SMA (see table 1) the most frequent type of SMA confirmed with molecular diagnosis, among the patients referred to our center, was type II SMA. We concluded that from all the studied samples that were sent by clinical geneticists, the 50% of the samples were positive for deletion of the 7 exon of SMN1 gene; being the PCRSA-RT technique a reliable test to diagnose SMA since it had a perfect correlation with the MLPA technique. In conclusion, the work realized makes a remark between the effort made by public institutions and patient registries associations to get to know genetic diseases like SMA.



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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

A NOVEL MUTATION IN RP1 IS A MAJOR CAUSE OF AUTOSOMAL DOMINANT RETINITIS PIGMENTOSA IN SOUTHERN ITALY

AUTHORS

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ABSTRACT

Retinitis pigmentosa (RP) is the most common form of inherited retinopathy, affecting more than 1.5 million people worldwide. RP constitutes a heterogeneous group of inherited degenerative retinal diseases characterized by progressive loss of photoreceptor function resulting in night blindness, reduced peripheral vision, decreased visual acuity, abnormal retinal electrophysiology, and pigmentary retinopathy (1). To date, more than 20 different genes have been associated to autosomal dominant retinitis pigmentosa (ADRP), but they account for only 50% of cases worldwide (2). We performed molecular analysis of the major ADRP genes, namely rhodopsin (RHO), peripherin 2 (PRPH2), retinitis pigmentosa 1 (RP1) and con-rod homeobox containing gene (CRX), in 130 Italian families affected by ADRP. Moreover, to further increase ADRP diagnostic sensitivity, we also analyzed by DNA sequence capture a large panel of genes associated to inherited eye diseases in three ADRP patients without mutations in RHO, RP1, RDS and CRX. Coding regions of RHO, PRPH2, CRX and exon 4 of RP1 were analyzed by Sanger sequencing. A panel of 260 genes was selected and used to obtain a custom array for target enrichment. Next-generation sequencing was carried out on the Roche 454 Genome Sequencer instrument (3). In 17 ADRP families (13%), we identified eleven different potentially pathogenic mutations. In our ADRP patients, the relative involvement of RHO (6%) and PRPH2 (<1%) is lower than in US and UK. In contrast, about 7% of our patients have mutations in RP1. Surprisingly, a single, novel, nonsense mutation in RP1 (p.S740X) accounts for about 4% of our cases and therefore can be considered a major cause of ADRP at least in Southern Italy. The next generation sequencing screening identified putative pathogenic variations in all three analyzed patients. Despite the wide genetic heterogeneity in Italian patients, our data suggest that priority should be still given to the analysis of RHO and RP1. Moreover, our extended analysis strongly indicates that advanced, high-throughput technologies for molecular screening of ADRP-associated genes are warranted for speed and cost-effective reasons.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

BBS1, BBS10 and BBS2 are major causative genes for Bardet-Biedl syndrome in Italian patients.

AUTHORS

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ABSTRACT

Bardet-Biedl Syndrome (BBS) is a rare inherited disorder associated with obesity, retinopathy, renal defects, polydactyly, learning disabilities and hypogonadism. Seventeen genes account for about 80% of the known cases of BBS, indicating that additional BBS genes are yet to be identified. BBS prevalence is 1 in 125.000–160.000 in Caucasian people. The wide clinical spectrum observed in BBS correlates to the high genetic heterogeneity (1). Usually, BBS is transmitted in autosomal recessive manner. However, in some families, a triallelic inheritance involving BBS1, BBS2 and BBS6 genes has been observed (2). To design a sensitive and time-effective procedure for molecular diagnosis of BBS, we analyzed a cohort of 21 Italian patients. First, we used the APEX genotyping microarray (Genorama) to search for 300 known mutations in 11 BBS (BBS1-BBS10, BBS12), in PHF6, ALMS1, and GNAS1 genes. Then, we analyzed by direct sequencing the whole coding regions of the BBS1, BBS2 and BBS10 genes, in patients who resulted with one and without a mutation after APEX analysis. The genotyping microarray identified both mutated alleles in 5 patients and one mutated allele in 1 patient, for a total of 11 disease-alleles (6 in BBS1, 3 in BBS10 and 2 in BBS2), yielding a detection rate of about 26.2% (11/42). In addition, sequence analysis allowed us to identify 8 new mutations, 3 in BBS10 (1 point insertion, 1 missense and 1 nonsense mutation), 4 in BBS2 (2 missense, 1 point insertion and 1 point deletion) and 1 missense mutation in BBS1. The detection rate of the whole procedure increased to 45,2%. Our study indicates that sequencing of BBS1, BBS2 and BBS10 should be chosen as first analytic step in the molecular diagnosis of BBS in Italian patients. The subsequent analytical step might be the APEX array. Obviously, in the complex framework of the molecular diagnosis of BBS, next generation sequencing analysis would be strongly recommended.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

The experience of the Nation-wide Italian Collaborative Network of Mitochondrial Diseases

AUTHORS

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ABSTRACT

Mitochondrial disorders are among the most common genetic disorders. In contrast to the extraordinary progress in our understanding of the molecular bases, we are still extremely limited in our ability to treat these conditions. Small patient populations represent the major impediment to progress. The development of a web-based register of patients with mitochondrial disease is needed to better understand the phenotypes and the natural history of these diseases. Eleven centers with expertise on mitochondrial medicine have been involved in this project. To date, we have collected 1160 patients, with both adulthood and childhood onset. The network has reached the following goals: 1. establishment of an Italian network with specific expertise; 2. creation of a validated web-based database (supported by Telethon GUP09004), harmonized with other European databases and networks; 3. characterization of a big cohort of cases. Our database allows many phenotype-based and genotype-based studies. Two examples are given: - Phenotype-based approach: exercise intolerance. More than 20% of patients complained of exercise intolerance. This symptom was more strongly associated with specific mutations (i.e., 3243A>G). CK levels were increased in ~34% of the patients with exercise intolerance, not confirming the notion that CK are normal in mitochondrial patients. Moreover, all the other myopathic signs included in our database were associated with exercise intolerance. Ragged red fibers and, especially, COX-negative fibers were more frequent in the subjects with exercise intolerance, whereas lactate levels could not predict the presence of exercise intolerance. - Genotype-based approach: the 8344A>G mutation in our database. Myoclonic epilepsy with ragged-red fibers (MERRF) is a rare mitochondrial syndrome, mostly caused by the 8344A>G mitochondrial DNA mutation. 42 patients carrying the 8344A>G mutation were identified. Myoclonus was present in one out of five patients, whereas myopathic signs and symptoms, generalized seizures, hearing loss, eyelid ptosis and multiple lipomatosis represented the most common clinical features. Our results showed higher clinical heterogeneity of the 8344A>G mutation than commonly thought. Moreover, MERRF could be better defined as a myoclonic ataxia rather than a myoclonic epilepsy. Large, multicenter studies are strongly needed to better characterize the

clinical picture and natural history of these diseases, in order to identify some countermeasures capable of benefit the patients suffering with these chronic, still incurable disorders.

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N. 49

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

GH TREATMENT, BMI AND DIFFERENT GENOTYPES IN PATIENTS WITH PRADER-WILLI SYNDROME AND SCOLIOSIS: IS THERE ANY RELATIONSHIP ?

AUTHORS

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ABSTRACT

The purpose of this study is to develop a protocol defining a clinical diagnostic procedure for the patients to be admitted to the authors' Institute to receive treatment for either suspected or confirmed diagnosis of spine deformity in Prader-Willi syndrome. The aim is to evaluate every subject from the diagnostic point of view, assessing variability of clinical expression and evolution of spinal deformity in the light of the related genetic aspects, thus providing a univocal protocol. The present series only includes patients (18 cases) with Prader-Willi syndrome, 7 hospitalized for surgical treatment of scoliosis, 11 followed-up at the authors' institute only for conservative treatment of scoliosis. Both BMI tracks (weight/height²) and BMI Z-score (only for children older than 2 years) were assessed. Moreover, the GH treatment was evaluated for each group of patients as follows: being administered, suspended or no treatment. Finally, the gene was compared with BMI. No relationship was observed either between GH treatment and mean BMI or between genetics and mean BMI. More patients should be seen by the Authors to confirm or refute the current findings.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Diagnosis rate of alpha-1 antitrypsin deficiency (AATD) in Spain: geographical differences based on reports to the Spanish Registry of Patients with AATD (REDAAT)

AUTHORS

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ABSTRACT

Introduction: Severe alpha-1 antitrypsin deficiency Pi*ZZ type is a rare hereditary disorder in Spain, with an estimated prevalence of 1: 3,334 individuals, and about of 12.000 carriers of this deficient genotype. Severe deficient subjects often suffer from COPD, chronic liver diseases, and exceptionally relapsing panniculitis or systemic ANCA+ vasculitis. Nevertheless, one third of them will never show clinical symptoms. A high rate of under-diagnosis of AATD has been reported all over the world, usually being attributed to a lack of awareness of its existence among care givers as well as to the misunderstanding of symptoms leading to wrong diagnoses. The REDAAT collect data from patients affected by severe AATD from 1993 with scientific proposals. Volunteer physicians from all country should register their cases in the REDAAT database (www.redaat.es). This study describes the detection rates among different regions of Spain based on REDAAT database. Results: A total of 480 patients (294 -61%- males) are included at REDAAT, this figure being only a 4% of all expected affected individuals in Spain. The mean age of these enlisted subjects is 56 (SD: 15.7). Impairment of lung function is relevant in our population, with a mean FEV1 0,98L (SD: 1.3) and FVC 2,1 L(SD:1,9); 7% of these enlisted subjects died during the follow-up period, generally by respiratory or liver insufficiency. The mean detection rate considering a prevalence of 33 affected individuals/100.000 inhabitants is of 1 case/100.000, but a wide range from 0.1 to 6,6 is observed. Conclusion: As well as in other countries, both under-diagnosis and non-notification of AATD detected cases to the Patient's Registry constitutes a major problem in our Country. Besides, we also found remarkable differences in notification of cases rate among the 17 Autonomous Communities existing in Spain. Since these differences in notification cannot be explained by epidemiological differences of the disorder prevalence, specific programs aimed to improve awareness about AATD among people from these regions and supporting for diagnose would need to be implemented.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Causes of mortality among patients with alpha-1 antitrypsin deficiency from the Spanish Registry REDAAT

AUTHORS

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ABSTRACT

Introduction: Alpha-1 antitrypsin (AAT) deficiency is a genetic disorder that causes conformational alterations of the AAT structure provoking polymerization of misfolded proteins into hepatocytes, and secondary reduction of the AAT blood levels leading to insufficient antiprotease activity in lungs, both of these facts favoring the development of liver diseases (usually liver cirrhosis and hepatocellular carcinomas) as well as COPD (typically, pulmonary emphysema). Since 1,993, REDAAT collects data from adults with severe AAT deficiency (AATD), in order to improve the knowledge of the natural history of this uncommon genetic disorder. The REDAAT database includes a total of 476 subjects, with the following Pi (protease inhibitor) phenotype/genotype distribution: Pi*ZZ 351 (74%), Pi*SZ 112 (23%) and rare or null deficiency variants 13 (3%). In this report, the available causes of mortality and demographic characteristic of patients enlisted in the REDAAT who died during the follow-up period 2,001-2,013 are described. These data are available on line at the REDAAT database (www.redaat.es) **Results:** Forty-eight individuals, 36 of them males, died during the 12-year follow-up period. The vast majority (i.e., 43) of these deceased patients showed Pi*ZZ phenotypes, 4 were Pi*SZ, and 1 carried a Pi*Null genotype. AATD was detected in these patients due to COPD in 40 (83%), because liver cirrhosis in 6 (12.5%), and by family screening in 3 (6.25%). Most Pi*ZZ and Pi*SZ subjects were current or former smokers, while the null patient never smoked. Liver cirrhosis and COPD caused 15 (31%) and 11 (23%) deaths respectively. A miscellanea other less frequent causes of death were: multi-organic failure after lung transplantation (2), non-lung cancers (3); dementia (1); major bleeding (1); sudden death (1); sepsis (1); heart failure (1); post-surgical complications (1). In 11 cases the cause of death was not reported. With exception of one case, never smokers died by conditions different of COPD. **Conclusion:** Our descriptive study found a notable liver cirrhosis-related mortality rate among Pi*ZZ and Pi*SZ subjects. A quarter of deaths were related to COPD, and seemed strongly linked to the Pi*Null genotype, as well as to Pi*ZZ and Pi*SZ types with smoking habits.

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Rare cancers in Mallorca

AUTHORS

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ABSTRACT

Objetive. To describe the rare cancers diagnosed in 2005 in the population of Mallorca. **Methodology.** The rare cancers are defined as those with an incidence lower than 6 per 100.000 inhabitants. The classification used by the Rare Cancer European Surveillance is based on their topography and histology through the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3). The Rare Diseases Registry of the Balearic Islands is a population based registry that includes all the rare cancers recorded in the Cancer Registry of Mallorca. The population in Mallorca in 2005 was 777.821 inhabitants. We describe the rare cancers diagnosed in 2005 in Mallorca and their status in 2012. **Results.** The total number of recorded cases was 1,129, (52.9% in women). The average age at the diagnosis was 61 years (0-97) in women and 64 (0-99) in men. The most frequent location (25.2%) was digestive (C15-25); mainly gastric (21.8%) and among them the pyloric antrum adenocarcinoma (33.9%). The following in frequency were the liver and biliary tract cancer (17.6%) and pancreas (16.2%). Males have a higher incidence of aesophagic cancer (47.3%) and females of gallbladder (86.7%). The second cancer in frequency are those of female genital organs (C51-58) (23.7%) and the cervix cancer not specified (C539) among them (51.5%). Men have more digestive cancer [29.5%], respiratory and intrathoracic [22.7%], while women's most frequents cancers are those of genital organs (44.9%) and digestive (21.3%). In December 2012, 474 patients (42%) had died, 56% of them men (268). The average of the age of death was 68 years in men and 74 in women. **Conclusions** The more frequent rare cancers are digestives: gastric, liver and biliary tract. The average of the age at diagnosis is similar in both sexes, while the death was higher in women. It is necessary to further analyze and study rare cancers incidence and survival and integrate their data in the Population Registry of Rare Diseases of the Balearic Islands. **Keywords.** Rare cancers. Population Registry.

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N. 53

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

PosterTitle Hospital admissions of patients with thalassaemia in the Balearic Islands

AUTHORS

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ABSTRACT

Objective Some thalassaemias, specifically β thalassaemia, are more common in the Mediterranean populations. The analysis of the hospital admissions records can help to know the presence of the disease in the Balearic Islands. The aim of this study is to describe the patients with thalassaemia admitted to public hospitals of the Balearic Islands in 2010. **Methodology** Descriptive analysis of the cases of thalassaemia admitted to public hospitals in the Balearic Islands in 2010. The data were obtained from the Minimum Data Set (MDS) after hospital discharge of patients with a diagnosis of thalassaemia in any of the in the MDS fields C1-C13 which are encoded by the International Classification of Diseases 9th edition (ICD-9 CM). The codes included were 282.4 (thalassaemia), 282.41 (sickle-cell thalassaemia without crisis), 282.42 (sickle-cell thalassaemia with crisis), 282.49 (other thalassaemias) and 282.5 (sickle-cell trait). **Results** The patients admitted in the public hospitals of the Balearic Islands in 2010 with a diagnosis of thalassaemia at discharge were 209, 61.7% of them female. The median age was 56 years (0-90) in female and 64 in male (2-96). The diagnosis were "other thalassaemia" (ICD-9: 282.49) in 67.0% of patients, "sickle-cell thalassaemia without crisis" (ICD-9: 282.41) in 31.6%, followed by "sickle-cell trait" (2 cases) and "sickle-cell thalassaemia with crisis" (1 case). The distribution by gender is identical in "other thalassaemia" and "thalassaemia without crisis", 37.9% men and 62.1% female. The lower median age was in patients with "thalassaemia without crisis", 25 years in male and 41 in female. Fourteen patients (6%) died in the hospital, 57% of them male. The median age was of 78 years (37-90) in male and 81 (70-95) in female. **Conclusions.** The most frequently diagnosed thalassaemias in the Balearic Islands are "other thalassaemias" including among others Cooley's anemia, Mediterranean thalassaemia, Hb-Bart's disease, thalassaemia α , and thalassaemia β . For a more accurate study of thalassaemia, in particular of β thalassaemia, through the MDS data it is necessary to disaggregate the ICD-9 CM codes of thalassaemia in each one of the included diseases. It is advisable to continue the study to analyze the prevalence in the Balearic Islands. **Keywords.** Thalassaemia, Minimum Data Set, Rare disease

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ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

SURVEILLANCE PROGRAMS IN HEREDITARY COLORECTAL CANCER SYNDROMES: PRELIMINARY DATA FROM A RARE DISEASE REGISTRY

AUTHORS

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ABSTRACT

INTRODUCTION: The major hereditary colorectal cancer syndromes (HCCS), Lynch syndrome (LS), Familial Adenomatous polyposis (FAP) and Mutyh Polyposis (MAP) predispose to early onset colorectal (CRC) and extracolonic malignancies (EC). A major concern for clinicians is the definition of cancer surveillance programs (CSP). Few prospective studies are available and the optimal strategies, timing for surveillance, spectrum of EC associated is still undefined. **AIMS:** to define HCCS-associated EC; to evaluate the efficacy of CSP in the affected. **METHODS:** From April 2008, data of patients (pts) who refer to the Cancer Family Clinic of our Institute with LS, FAP or MAP, are recorded in the Lazio Rare Disease Registry. All patients are included in a CSP. FAP/MAP pts undergo: side viewing gastroscopy and videocapsule endoscopy (VCE) every 3 years by the age of 20; thyroid ultrasound (US) every year by the age of 15; abdominal TC or RMN every 3 years by 1 year after colectomy. LS affected undergo by the age of 30: endoscopic upper US or abdominal TC for pancreato-biliary surveillance, urine cytology, dermatological screening, transvaginal US with endometrial sampling, breast US and mammography every year; gastroscopy and VCE every 3 years. **We report an "ad interim" analysis of the data after 5 years of follow-up.** **RESULTS:** We recruited 86 FAP (44M/42F), 17 MAP (11M/6F) and 71 LS (33M/38F). We did not detect any EC in MAP. In the 86 FAP we observed: 10 duodenal adenomas (11,6%); 3 jejunal adenomas (3,5%); 5 thyroid papillary cancers (PTC)(4,3%); 6 intrabdominal desmoids (ID) (6,9%), one of which was aggressive and required chemotherapy. In the 71 LS we detected: a cholangiocarcinoma, an ureteral carcinoma and a sebaceous skin carcinoma, These four cases carried a MSH2 gene mutation. **CONCLUSION:** In our MAP series we did not observe EC. In 4,3% of FAP cases we found PTC, vs 1-2% reported in other studies. These data seem to justify US screening. Once a year appeared an adequate timing. 6,9% of FAP had ID, less than reported in FAP cancer registries studies (20%). In our LS series, we did not find any endometrial cancer, the second most common cancer of the syndrome. We observed EC only in MSH2 gene mutation carriers. If these data will be confirmed on a larger series and longer surveillance, a tailored and more intensive surveillance could be justified in MSH2 rather than MLH1 gene mutation carriers.

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N. 55

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Molecular epidemiology of childhood neuronal ceroid-lipofuscinosis in Italy

AUTHORS

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ABSTRACT

Neuronal Ceroid Lipofuscinoses (NCL) are clinically and genetically heterogeneous, inherited neurodegenerative diseases with worldwide distribution. They are childhood diseases; rare adult onset forms are known. NCL have a progressive course, affecting visual, motor and cognitive functions, and are associated with myoclonic epilepsy; behavioural problems can be observed at the onset. The outcome is invariably fatal, mostly during the second or third decade. The denomination is based on pathological criteria, i.e. the presence of intralysosomal storage of autofluorescent lipopigment with characteristic ultrastructural features. The NCL are autosomal recessive diseases (but a rare autosomal dominant form of adult onset). Thirteen NCL genes have been identified so far. In this study we have reviewed the descriptive epidemiological data on neuronal NCL in Italy, identified the spectrum of mutations in the causative genes, and analyzed possible genotype-phenotype relations. A cohort of NCL patients was recruited through CLNet, a nationwide network of child neurology units sharing common diagnostic algorithms. Diagnosis was based on clinical and pathological criteria following ultrastructural investigation of peripheral tissues. Molecular confirmation was obtained during the diagnostic procedure or, when possible, retrospectively. One hundred eighty-three NCL patients from 156 families were recruited between 1966 and 2010; 124 of them (from 88 families) were tested for known NCL genes, with 9.7% of the patients in this sample remaining genetically undiagnosed. Late infantile onset NCL (LINCL) accounted for 75.8% of molecularly confirmed cases, the most frequent form being secondary to mutations in CLN2 (23.5%). Juvenile onset NCL patients accounted for 17.7% of this cohort, a smaller figure than in other European countries. Gene mutations predicted severe protein alterations in 65.5% of the CLN2 and 78.6% of the CLN7 cases. An incidence rate of 0.98/100,000 live births was found in 69 NCL patients born between 1992 and 2004, predicting 5 new cases a year. Prevalence was 1.2/1,000,000. Descriptive epidemiology data indicate a lower incidence of NCL in Italy as compared to other European countries. A relatively high number of private mutations affecting NCL genes might explain the genetic heterogeneity. Specific gene mutations were associated with severe clinical courses in selected NCL forms only. The enhanced knowledge of the epidemiology of NCL in Italy, particularly the figures of prevalence and the prediction of new cases per year, will contribute to improve the awareness of each form specificities. That should help a better allocation of health resources for planning care in children and their families.



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N. 56

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Mexiletine:pharmaco-epidemiological study

AUTHORS

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ABSTRACT

In March 2010 Boehringer Ingelheim Italia definitely stops the production of Mexitil[®] (mexiletine) by not renewing the marketing authorisation (AIC in Italian). The drug becomes unavailable on the market because no other suppliers are available. No analysis of the consequences for myotonic patients is carried out because the clinical use for these conditions is off-label. The joint intervention of the Military Chemical and Pharmaceutical Factory established in Florence (in Italian SCFM), the Italian National Institute of Health (in Italian ISS) and the Italian Medicines Agency (in Italian AIFA) have reached the goal of reintroducing this pharmaceutical product in a short time. The special rules of prescription and dispensation have allowed, for the first time, to carry out a detailed pharmaco-epidemiological study. The number of patients treated is 665, of which 200 are affected by a form of myotonia. It has also been analysed the regional distribution of the treated patients and the origin of the prescriptions. This study highlights the role of public institutions in enforcing the right of people affected by rare diseases to receive an adequate treatment.

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N. 57

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

SPANISH FAMILIAL PANCREATIC CANCER REGISTRY AND SCREENING OF HIGH-RISK INDIVIDUALS.

AUTHORS

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ABSTRACT

Background: Familial Pancreatic Cancer (FPC) is an autosomal dominant rare syndrome defined as families with two or more first-degree relatives with pancreatic cancer that do not fulfill the criteria of any other inherited tumor syndrome. Approximately, 15–20% of families carry germline mutations in BRCA2, PALB2 and ATM, for the majority of families the major underlying genetic defect(s) are unknown. The Spanish familial pancreatic cancer registry, Pan-Gen-FAM was established in 2008 in order to identify and manage families at high risk of developing PC. Materials and Methods: The phenotype of families is studied using family history information to determine whether they present PC alone or in combination with other cancer syndromes. The main objectives of this project include the identification of novel mutations or variants that predispose to an increased risk of PC by DNA exome ultrasequencing of both tumor and germline DNA. Furthermore, we offer a clinical follow-up program of high risk individuals with a screening program for the detection of early PC lesions consisting of periodic monitoring by imaging techniques (EUS, CT and MRI) and the evaluation of minimally-invasive tumor biomarkers approaches Circulating Tumor Cells (CTC) and micro RNAs. Results: To date the registry includes over 100 individuals representing some 36 families presenting with pancreatic cancer aggregation. The most frequent abnormal findings were parenchymal changes associated with chronic pancreatitis (hyperechoic foci, echogenic strands, lobularity, cysts, pancreatic heterogeneity). Overall 14 (39%) patients showed at least 1 of these changes. Two lesions were compatible with a mucinous tumor. A well differentiated neuroendocrine tumor in one patient. All patients with cystic lesions are undergoing close clinical observation. One CTC was detected in one patient, although this was consistent with the false negative detection rate of the system. No results of DNA exome ultrasequencing or microRNAs are yet available. Conclusions: This study is the first Spanish registry of familial pancreatic cancer and it is due to a multidisciplinary team involves both clinical and basic scientists and epidemiologist.

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N. 58

ABSTRACT TYPE

Poster: *Case-Studies*

TITLE

Cystic fibrosis mortality trends in Spain from 2005 to 2011

AUTHORS

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ABSTRACT

Background/objective: Cystic fibrosis (CF) is a rare disease that mainly affects the respiratory and digestive systems. Exocrine gland secretions are thicker and more difficult to eliminate, facilitating local inflammation and infection where they lie. Pulmonary disease remains the leading cause of morbidity and mortality in patients with CF. A previous study of CF mortality in Spain during the period 1981-2004 revealed a descendent trend from 1981 to 2002 and an ascendant trend from 2002 to 2004. The objective of this study was to analyse whether the ascendant CF mortality trend observed from 2002 to 2004 continue increasing from 2005 to 2011. Materials and methods: Data on deceased of CF at age 0-29 were drawn from the National Statistics Institute. Crude and age-standardised CF mortality rates were calculated, overall and for each gender. Joinpoint regression models were used to describe changes in trend from 1981 to 2011 (data from 1981 to 2004 came from a precedent study). Age specific mortality rates, overall and by gender, were assessed for deceased at less than 1, 1-14 and 15-29 years old. Percentage of deceased in each age group was calculated. Results: The crude CF mortality rates in 1981, 2004, 2005 and 2011 were, respectively: 2.05, 1.44, 1.34 and 1.17 per million in men and 2.18, 1.79, 1.20 and 1.85 per million in women. Considering age-standardised CF mortality rates of the whole period (1981-2011), a statistically significant decrease from 1981 to 2001 and a statistically significant increase from 2001 to 2011 was observed in both sexes. A change in the age of death was observed between the two periods: from 1981 to 2004 most people died at age 1-14 whereas from 2005 to 2011 most people died at age 15-29. Discussion: The CF mortality trend suffered a change in 2001: it decrease from 1981 to 2001 and increase in the last decade. Nevertheless, people with CF die older and older: at age 1-14 during 1981-2004 and at age 15-29 during 2005-2011. Our study is descriptive and it not allows to know the causes of observed changes. The mortality increase could be due to the fact that CF screening programs started at 1999 in Spain, what improved CF detection and implied that more people died with a diagnosis of CF.





ORAL PRESENTATIONS



N. 59

ABSTRACT TYPE

Oral Presentations

TITLE

The Paroxysmal Nocturnal Hemoglobinuria Registry

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ABSTRACT

The Italian Database for Paroxysmal Nocturnal Hemoglobinuria (IDPNH) was set up in 2010 by the Italian Centre for Rare Diseases of the Istituto Superiore di Sanità (ISS). The database is meant to include all patients with PNH: there are no exclusion or inclusion criteria other than a diagnosis of PNH established according to current international standards. The main aim of the Database is to enhance our knowledge of the natural history of the disease, and to obtain short-term and long-term data with respect to how they respond to available treatment measures. The Database was made possible by the willing cooperation of (i) ISS staff, (ii) hematologists with specific experience in the diagnosis and management of PNH and (iii) representatives of the patients association AIEPN. In the course of several joint meetings of these 3 groups a set of variables were considered in specific areas, including: personal data, clinical data, diagnostic tests, other laboratory data, blood transfusion treatment, drug treatment, pregnancies, quality of life. The Database is web based, and personal data are encrypted according to national regulations on the protection of personal data. Data are entered by individual haematologists who are in charge of PNH patients and who have received appropriate credentials. When the data set for an individual patient are complete, they are validated by a national expert on PNH. The PNH Database interfaces with the Italian National Registry for Rare Diseases (INRRD) which, since it was established in 2008, includes data on 485 rare diseases. IDPNH has now data on over 100 patients, which is still short of the total number of PNH patients living in Italy: therefore a priority objective is to ameliorate coverage. Validation rate has been greater than 80%, indicating that diagnosis and clinical assessment are generally good to excellent. The Italian Registry is at the moment unique, in terms of being (a) public, (b) comprehensive with respect to clinical and laboratory data, (c) unbiased with respect to patient entry. We now have a good basis for cross-sectional and, even more important, longitudinal studies on PNH.

N. 60

ABSTRACT TYPE

Oral Presentations

TITLE

ALPHA1 INTERNATIONAL REGISTRY : A REGISTRY FOR ALPHA1-ANTITRYPSIN DEFICIENCY

AUTHORS

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ABSTRACT

Alpha1- antitrypsin deficiency (AATD) is an inherited condition characterized by reduced level of circulating alpha1-antitrypsin (AAT), associated with increased risk of developing obstructive lung disease (COPD), mostly pulmonary emphysema, early in life, and chronic liver disease, in later phases. First recognized fifty years ago in Sweden, AATD is now considered the commonest rare respiratory disorder, with an estimated prevalence of 33/100,000 individuals (including carriers). At the end of the last century, WHO suggested that knowledge of epidemiology and natural history of the disorder would have benefited for the development of an international registry, deriving from the collaboration of singles national registries. To comply with such recommendation, twenty national AATD registries from four continents developed a common data collection form to enter clinical records of patients with the two commonest AATD deficiency genotypes, i.e. PI*ZZ and PI*SZ, and other rare AATD genotypes associated with severe deficiency of plasma levels of AAT (< 50 mg/dL or 11 μ M). The Alpha1 International Registry (AIR) was established in 1996, and since then AATD subjects were prospectively enrolled. Updated August 2013, a total of 4,383 AATD individuals were recorded. Austria, Canada, Denmark, Germany, Italy, the Netherlands, New Zealand, Spain, Sweden, and United Kingdom enrolled more than 100 AATD individuals each. PI*ZZ genotype accounts for 85% of enrolled subjects, PI*SZ for 11 %, whereas the remaining 4% is represented by rare AATD genotypes. Patients enrolled for lung disease account for 60%, whereas those enrolled for liver disease account for 6%. Fifteen % were healthy subjects, most likely detected during family screening (relatives of index cases), whereas of interest is the finding that 20% of enrollees are affected by either lung and liver disease, a figure more relevant than previously believed. When subjects were stratified in function of the genotype, interestingly we notice that healthy individuals are not present among Null genotypes, thus further supporting the concept that the risk for COPD in AATD is inversely related to the level of circulating AAT. The AIR is a powerful tool for improving the knowledge of AATD.

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N. 61

ABSTRACT TYPE

Oral Presentations

TITLE

Why developing an orphan drugs registry?

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ABSTRACT

Registries and databases are key tools to increase knowledge on rare diseases and facilitate research¹. Many registries focused on rare conditions exist, while databases on orphan drugs are still needed². EuOrphan is a free and regularly updated database including 'orphan drugs' (ODs) designated and marketed by EMA and by FDA. The database collects information from EMA /FDA official sources³. The following information is collected: active substance, sponsorship, designation date, orphan condition(s), orphan indication(s), disease area, genetic and paediatric status. In case of approved drugs, administrative data, approved therapeutic indication, approved paediatric ages, clinical studies supporting the Marketing Authorisation (MA) are also stored. The main objectives of EuOrphan are: a) to measure the coverage of the therapeutic needs of rare diseases patients in Europe; b) to analyse the level of existing evidence on efficacy/effectiveness at the time of the MA. **Methods** Information on designated and approved ODs by FDA have been used to develop comparative statistics and evaluations. **Results** Results are synthesised below: on June 1st 2013, 860 orphan designations were released from EMA (an average of 68,8 by year since 2000) and 1889 from FDA (an average of 62,97 by year since 1983). On a total of 1179 orphan conditions provided by both the Agencies, 356 are genetic, 948 affect the paediatric population. No substantial differences were observed by therapeutic area. A total of 278 active substances received a Orphan Drug MA in US covering 239 orphan conditions. In Europe today 62 medicines result in the ODs Community Register, while additional 98 medicines are authorised to be used in an orphan indication (13 no more present in the ODs register and 85 approved before the OD Regulation entered into force). MAs were based mainly on flexible level of evidence and reduced number of trials. Among the considered medicines, only 60 are approved with the same (or similar) indication both in Europe and US, while 100 and 218 orphan medicines are marketed only in Europe and US respectively. **Conclusions** Our results show that the patient needs coverage could be increased by merging registrative and efforts for clinical trials at EMA and FDA level and that OD registries including data we presented could be of help in focusing these efforts in the right way. Conclusively, on the basis of these characteristics, EuOrphan demonstrates to represent a relevant source of information, not available otherwise, to be used by experts, regulators and patients.

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ABSTRACT TYPE

Oral Presentations

TITLE

Feasibility of Common Data Elements (CDEs) among RD Registries: results from the EPIRARE Survey on Common Data Elements.

AUTHORS

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ABSTRACT

EPIRARE (Building Consensus and synergies for the EU Registration of Rare Disease Patients), is a three-year project, co-funded by the European Union. Its aim is to elaborate a proposal for a European Platform for Rare Disease (RD) Registries intended to improve the use of RD patient data, promote standardisation of data collections, support the registration of patients and the use of data for research and public health purposes. In order to assess the feasibility of common sets of data elements the project carried out a web-based survey, between February and April 2013, addressed to a list of regional, national and international RD and orphan drug registries. The survey inquired on more than 50 data elements likely to be collected by Registries, regarding: registry aims, patient's personal data, clinical and genetic disease data and comorbidity, data on: diagnostic and treating Centres, orphan and common drugs and other treatments, patient's interest in clinical trials and biological donations, transplants, link to biobanks. The survey considered the definitions of the US GRDR on CDEs and adapted them to the European context. Out of 180 responses, we analysed 147 records using the software EpilInfo. The main aims declared by Registries are: epidemiological research (86%), natural history of the disease (71%), drugs effectiveness (46%). According to the type of confirmed diagnosis, geographic coverage and data completeness, registries may be able to make estimates on: "incidence" (52%) and "prevalence" (52%), "life expectancy" (59%), "survival time" (48%), "diagnostic delay" (45.5%), "patient migration for diagnosis" (52%) and for treatment" (48%), patient willingness to be contacted for donating biological sample (38%) and participating in a future clinical trial (29%), "link to biobanks" (20%), "disability" (7%), "quality of life" (13%), "orphan drug use" (29%), its "effectiveness" (33%) and its "safety" (20%), "current drugs effectiveness" (27%), "information on other type of treatments" (59%): surgery (48%), cognitive (5%), physio (15%) and other rehabilitation (27%). The survey results show that most Registries currently collect data as proposed by the EPIRARE questionnaire and may be used in their current form to be shared within the platform to support public health policies and research. Acknowledgements: this work has been co-funded by the European Union within the framework of the Community Action Program on Health (Grant n. 20101202).

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ABSTRACT TYPE

Oral Presentations

TITLE

The Coordination of Rare Diseases at Sanford (CoRDS) patient registry for all rare diseases

AUTHORS

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ABSTRACT

BACKGROUND The Sanford Children's Health Research Center at Sanford Research has established a rare disease registry named CoRDS (Coordination of Rare Diseases at Sanford). CoRDS houses contact and clinical information contributed by individuals who have been diagnosed with any rare disease or awaiting diagnosis. CoRDS' mission is to accelerate rare disease research by creating a resource of de-identified data to researchers and a mechanism by which registry participants may be notified about research opportunities for which they are eligible. **METHODS** CoRDS is a rare disease registry with several components. First, there is a data collection component, in which informed consent and participant-reported data is collected online or by postal mail. CoRDS utilizes the Common Data Elements (CDEs) recommended by the Office of Rare Disease Research on its registry questionnaire. Second, data management involves the archiving, collation, and accumulation of data. Third, dissemination of data ensures that researchers can access data. A Scientific Advisory Board provides oversight, reviewing applications to ensure researchers have IRB approval. For its software solution, CoRDS uses Velos eResearch, a clinical research information system supporting the collection of data and processes in study design, monitoring, execution, participant recruitment, reporting, data integration, compliance and safety monitoring. Participant recruitment is closely tied to the process by which Patient Advocacy Groups (PAGs) partner with CoRDS. PAGs communicate enrollment information to their membership and educate their researchers about the opportunity to utilize CoRDS as a resource. CoRDS can customize registries so that PAGs may collect disease-specific data for their disease of interest. **RESULTS** CoRDS has 1478 participants (724 enrolled, 754 in screening), representing 147 rare diseases. CoRDS has partnered with approximately 50 PAGs and healthcare organizations that contribute to these enrollment metrics. On July 8, 2013, through a partnership with the National Ataxia Foundation, CoRDS launched the CoRDS Registry for the National Ataxia Foundation (NAF), a disease-specific registry for ataxias. **DISCUSSION** Collecting and collating data on patients diagnosed with any rare disease offers the opportunity to perform a comparative analysis to better understand and treat the diseases. Many treatments are symptomatic, thus treatment strategies for one disease may be beneficial in application to other diseases with similar clinical profiles. CoRDS serves as a source of data to help researchers better understand the particular disease they are studying and can help them identify potential participants for research studies or clinical trials with the potential to accelerate the timeline of research efforts.

N. 64

ABSTRACT TYPE

Oral Presentations

TITLE

The disease registries as instruments of knowledge and research in rare skeletal dysplasias

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ABSTRACT

Rare Skeletal Diseases (RSD) represent an heterogeneous group of hereditary connective tissue disorders presenting problematic aspects both in diagnosis and in treatment. The Medical Genetic Department (MGD) of Rizzoli Orthopaedic Institute (IOR), works on hereditary RSD from 2003 through a multidisciplinary day-clinic (genetic and clinical approach) and identify in Disease Registries the perfect instrument for solving most of constantly emerging problems. Currently the Multiple Osteochondromas Registry (REM) and Osteogenesis Imperfecta Registry (ROI) are actives. Primary aim of REM and ROI is the contribution to advancement of knowledge about natural history, epidemiology and molecular pathogenesis of MO and OI, and the pursuit of an upgrade in patient care and an improved quality of life (1). This idea has allowed, to this day, to collect clinical, genetic, genealogical and imaging data on a dedicated platform for more than 1000 patients with MO and more than 500 with OI, thus creating an amazing dataset of information for two orphan diseases. Moreover, identifying standard terminology reference and collecting data on an HL7 compliant platform, named GePhCARD (Genotype-Phenotype Correlation, Analyses and Research Database), REM and ROI simplify data sharing/merge and increase interoperability among institution, in order to further increase data on each Registry. As example, this instrument helps in arranging sub-cohort of patients, for deeper investigations and more accurate epidemiological analyses (2). The Registries in question, also pursue secondary purposes. In fact, the IT structure of platform that hosting patients data, can allow users to manage the integrated collection of molecular screening results as a mutational database. Moreover genetic investigations flanked by clinical data are the starting point for a genotype-phenotype correlation and for clinical research (3). Joined to this results, MGD created a collection of high quality biological materials, composed of various different categories of bio-samples (DNA, RNA, cell lines, tissue, blood and serum specimens, etc). Accessing the platform is possible to check the presence/absence of samples and define any further investigations of specific patients of family. Obviously dedicated personnel and proper infrastructures to adequately preserve data have been set (data are collected according to patient privacy rules and in agreement with current legal and ethical data protection requirements). To sustain the different needs of the two registers and the various skills required, the MGD is working in collaboration with national and international associations of patients affected by MO and OI.

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N. 65

ABSTRACT TYPE

Oral Presentations

TITLE

TOSCA, TuberOus SCLerosis Registry to IncreAse Disease Awareness: Registry Design

AUTHORS

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ABSTRACT

Tuberous sclerosis complex (TSC) is a multisystem, genetic disorder which affects both children and adults. This is a relatively rare disease with a birth incidence of 1:6000. Consequentially, there are gaps in the understanding of manifestations, interventions, and outcomes in patients with TSC. In 2011, medical experts and patient advocates, in collaboration with Novartis, evaluated the need for a TSC registry to address these gaps. There was a clear consensus to establish an international registry which resulted in the creation of Tuberous Sclerosis Registry to Increase Disease Awareness (TOSCA). Here we present methodological design of the TOSCA registry and the key objectives. TOSCA is a multicenter, international retrospective and prospective disease registry. Alive patients of any age with a diagnosis of TSC, documented visit for TSC disease within the last 12 months or newly diagnosed individuals are eligible for inclusion in the registry. Written informed consent will be obtained from all patients (or legal guardians) before enrollment. It is estimated that approximately 2000 patients will be enrolled from about 250 sites in more than 30 countries. More than 600 patients from 12 European countries have been included in the registry. Objectives include: to map the course of TSC manifestations and their prognostic role, to identify patients with rare symptoms and co-morbidities, to record interventions and their outcomes, to contribute to create an evidence base for disease assessment and therapy, to measure quality of life. "Core" section of the registry includes general information on patients' background, including demographics, family history, prenatal history, vital signs and disease features recorded at baseline and updated yearly. Subsections of the registry include additional data related to specific disease manifestations to be updated yearly. Initial enrollment period will be 24 months with a follow-up observation period of up to 5 years. A drug safety sub-study, TOSCA Post-Authorization Safety Study (PASS), will provide data for the European Medicines Agency to assess the long-term safety and tolerability profile of everolimus in the treatment of TSC patients residing in the European Union for the licensed indications. A Scientific Advisory Board, consisting of medical experts on TSC in the participating countries, patient advocacy group representatives and Novartis representatives, was set up for the general oversight of the scientific principles and conduct of the registry. Collaborative working is a key element of the registry. The information collected from this large cohort of TSC patients will inform future research in TSC.

ABSTRACT TYPE

Oral Presentations

TITLE

EUROMAC- European Registry of Patients Affected by McArdle Disease and other Rare Glycogenoses Presenting with Exercise Intolerance.

AUTHORS

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ABSTRACT

McArdle Disease (Glycogen Storage Disease Type V) is a rare inherited metabolic disorder affecting the skeletal muscle and is caused by mutations in the PYGM gene, which encodes the muscle isoform of glycogen phosphorylase. The main symptom is exercise-induced fatigue and painful muscle contractures, which sometimes can progress to rhabdomyolysis and myoglobinuria. Myoglobinuria can lead to kidney failure, which can be potentially life threatening. Currently, there is no treatment for this disorder, and there is only scarce data available on the epidemiology. Genotype/phenotype data on McArdle Disease are limited by small sample sizes. Based on the information gathered by existing European National registries, it can be estimated that this disorder affects approximately 3,000 persons throughout Europe. There is a global need for international cooperation on rare diseases, which is addressed by the International Rare Diseases Research Consortium (IRDRC). Twenty partners from 8 European countries have joined EUROMAC to set up a European registry for McArdle disease and other rare glycogenoses presenting with exercise intolerance as the main symptom, which include deficiencies in muscle phosphorylase b kinase, debrancher enzyme, muscle phosphofructokinase, phosphoglycerate kinase, phosphoglycerate mutase, muscle lactate dehydrogenase, beta-enolase and phosphoglucomutase 1. EUROMAC has been supported and funded by the Executive Agency for Health and Consumers and aims to identify as many patients as possible across Europe and to collect important natural history and epidemiological data from these patients. In the long run, EUROMAC attempts to improve genetic diagnosis by signposting relevant diagnostic laboratories. Standards of care will be developed, together with a plan to develop outcome measures for large multi-centre clinical trials. EUROMAC will stimulate public participation by actively involving patients and their caregivers, patients associations, clinicians, researchers and public institutions. This will be done by recruiting patients to fill the registry themselves on an online form prior to submitting a consent form. Data will be assigned a case code to ensure anonymity. A first set of minimum compulsory variables will include demographic data, symptoms, diagnosis methods and genetic data, while further optional details will cover more clinical and molecular data, treatment received, concomitant diseases and health-care services provided. We seek to recruit new collaborators and volunteers from both health services and patient support organizations. A workshop and a training course will take place from fall 2014 in Madrid to train patients and health



professionals on both clinical aspects and quality-of-life issues related to the diseases tackled in EUROMAC.

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ABSTRACT TYPE

Oral Presentations

TITLE

The Law's Role in Rare Disease and Orphan Drug Registries: Privacy and Data Protection.

AUTHORS

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ABSTRACT

Rare disease and orphan drug registries pose very interesting questions for public health governance. In an increasingly individualised medical landscape and society, concepts of solidarity and public interest become increasingly challenged and difficult to claim. Wide inclusion of citizens in medical research, especially research that uses genetic and other medical information, is desirable; where the maximum available cohort is small, participation becomes critical if research is to be successful. This poses the question: do those in these limited cohorts have different social responsibilities or rights expectations? In order to address this, the concept of privacy and the formulation of the concept of privacy need to be considered. In this paper, the objective nature of privacy will be challenged, and the need to focus on a more objective and philosophically robust 'public interest' appeal to citizens will be argued. From this, the potential for European data protection law to provide a legal framework to safeguard competing claims and interests in this area will be considered, with particular reference to the current developments in the reform of Directive 95/46/EC.

N. 68

ABSTRACT TYPE

Oral Presentations

TITLE

Analysis of the phenotypes in the Rett Syndrome Networked Database

AUTHORS

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ABSTRACT

Rett syndrome (RTT) is a severe neurodevelopmental disorder with one principal phenotype and several distinct, atypical variants (Zappella, early seizure onset, and congenital variants). The severity varies from mild to more severe phenotypes. There is only limited correlation between genotype and phenotype. The Rett syndrome networked database (RSND) is a unified repository of clinical and molecular data for RTT patients. It has been designed to allow researchers and physicians to access comprehensive patient information. RSND is currently the largest RTT database worldwide. It contains 1900 records of European and non-European RTT patients from 12 countries, entered by experienced clinicians to avoid ascertainment bias existing when questionnaires are sent out to families. These numbers can expand indefinitely. To protect sensitive data, patient records are de-identified. RSND is an open access initiative and data can be retrieved directly through a web-based search engine by all interested professionals We are providing here a description of the first 1900 records contained in the networked database and are discussing the content of RSND in the light of published guidelines for RTT, the development of clinical trials and with respect to other RTT cohorts.

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ABSTRACT TYPE

Oral Presentations

TITLE

International Registry of Steroid-Resistant Nephrotic Syndrome: updated epidemiological and clinical data

AUTHORS

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ABSTRACT

Introduction. Nephrotic syndrome (NS) is characterized by increased glomerular barrier permeability to plasma macromolecules resulting in heavy proteinuria. Minimal Change Disease (MCD) and Focal Segmental Glomerulosclerosis (FSGS) account for most of the cases. Glucocorticoids are first-line treatment, but despite adequate treatment remission is not achieved in 10% of MCD patients and in 60-80% of FSGS patients (Steroid-Resistant NS, SRNS). These patients are exposed to the risk of life threatening infections, thromboembolic episodes, dyslipidemia and 40% of them develop end-stage renal disease within 10 years from diagnosis. Genetic studies have shown that mutations in genes encoding proteins important for the podocyte homeostasis and function can cause SRNS. Gene mutations are found in about 60% of childhood-onset patients and in about 20% of adolescent- or adult-onset patients. In 2007 an International Registry dedicated to SRNS was established at the Clinical Research Center for Rare Diseases, with the following aims: - to collect clinical data of patients and their relatives; - to study genetic and biochemical abnormalities of SRNS; - to provide the best therapeutic approach for each patient. **Methods.** Clinical and laboratory data from patients with SRNS and available unaffected relatives are collected by a dedicated Case Report Form. Biological samples are stored from all participants. All participants receive detailed information on the purpose and design of the study and give their informed consent. Sanger DNA sequencing is performed. **Results.** Data and biological samples of 190 patients (104 sporadic and 86 familial cases) have been collected. Patients have been referred from 15 Italian Nephrology Units and 4 Units from other countries. Twenty-five percent of patients, who initially received isolated SRNS diagnosis, presented one or more extra-renal manifestations. We observed that familial cases have more frequently ear and eye involvement compared to sporadic cases, despite there was no statistically significant difference. Overall we found 23 patients with ear or eye manifestations (including the 4 with Alport disease diagnosis) suggesting that Alport or Alport-like syndrome may be underdiagnosed. Twenty-five patients presented steroid-dependent or multirelapsing NS. Within PodoNet consortium for podocyte diseases, we have studied adolescent-onset SRNS, a scanty characterized group. In our Registry 49 patients had mutations in WT1 (3/49), INF2 (2/49), CD2AP (1/49) and MYO11 (1/49). **Conclusions.** SRNS registry allowed epidemiologic, genetic and clinical studies. A better characterization of patients and a more accurate diagnosis were achieved. Finally, multicenter collaboration permitted a deeper knowledge of a very rare condition as adolescent-onset SRNS.

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N. 70

ABSTRACT TYPE

Oral Presentations

TITLE

eurIPFreg: A European Registry and Biobank for Patients with Idiopathic Pulmonary Fibrosis

AUTHORS

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ABSTRACT

Idiopathic pulmonary fibrosis (IPF) is a chronic lung disorder of unknown origin, manifesting with dyspnea, initially on exertion and later at rest, which ultimately leads to death. IPF is the most common form of idiopathic interstitial pneumonias (IIPs), a group of diseases caused by fibrosis or 'scarring' of the lung, hampering its proper function. The European IPF Registry and Biobank was born out of the EU 7th Framework Programme funded project European IPF Network (eurIPFnet). Aim of the eurIPFreg is the creation of a permanent and continuously growing record of well-defined data on IPF in Europe, in order to increase the chances of finding better treatment options for this devastating disease. Since its creation in 2008, eurIPFreg has become the largest database of longitudinal data from IPF patients, including control groups of patients with other lung diseases. Up to date 1018 participants (655 patients with IPF and other IIPs and 363 patients suffering from other lung diseases) from twenty-two different expert lung centers throughout Europe have been included in the eurIPFreg. Concomitant serial collection of blood, bronchoalveolar lavage, exhaled breath condensate and tissue with generation of a patient-, specimen-, and time-specific Lab-ID has been performed. In the frame of eurIPFreg, description of the natural course of IPF and other IIPs, especially with regard to environmental insults (professional and leisure activities, infections, other) has been conducted. Moreover, as part of the eurIPFnet project, extensive transcriptome, proteome and lipidome analyses were conducted that revealed a chronic endoplasmic reticulum (ER) stress-response in the alveolar epithelium. Research and infrastructural goals of the European IPF Registry include: a) Future development of non-invasive, air- or blood-borne biomarkers in IPF allowing safe diagnosis, sub-grouping of IPF subjects and identification of therapy-responders b) Quality of Life assessment c) Description of epigenetic changes in IPF lung epithelial cells and fibroblasts d) Whole genome profiling in IPF subjects e) Isolation of progenitor cells and different parenchymal cell populations from IPF and other lungs The eurIPFreg is characterized by a philosophy of collaboration and interoperability, making substantial efforts to increase patient involvement in its further development and to retain its financial autonomy through clearly established partnerships with public funding sources and the industry.

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N. 71

ABSTRACT TYPE

Oral Presentations

TITLE

Pharmacovigilance using patient registries

AUTHORS

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ABSTRACT

EU legislation requires post-authorization safety and efficacy surveillance, pharmacovigilance, for new drugs. For drugs targeting rare disease, the European Medicines Agency (EMA) asks the pharmaceutical companies to work with the patient registries in order to collect the data for the post-authorization safety and efficacy studies. This poses some practical as well as legal challenges. Practically, the data, especially for safety survey, must be collected in almost real time, otherwise severe side effects may go unnoticed for too long. Some registries only collect data on a yearly basis, and, in particular, for the European Cystic Fibrosis Society Patient Registry (ECFSPR), data are further delayed because, for some of the national registries, they need to be cleaned and reported nationally before being sent to the ECFSPR. Furthermore, the side effects surveyed will vary from drug to drug, and the amount of data for patients on several new drugs may be almost insurmountable. For efficacy surveillance, data on patients NOT on the studied drug will also be necessary for comparison, adding to the load of data. Legally, the data in the ECFSPR are governed by EU and national data protection legislation, including informed consents from the patients. Data can be used for e.g. quality control and research. Data use and ownership is determined the ECFSPR Guidelines and Terms of reference. Data collected for pharmacovigilance must therefore be governed in the same way, and cannot be just collected and handed over to the pharmaceutical company. We suggest working in close cooperation with the pharmaceutical companies and EMA setting up a collective data set that would cover general pharmacovigilance aspects with the possibility of adding specific variables for rare side effects. Contracts on handling, analyses and disclosure of data, including publication on EMA's Eudravigilance webpage <http://eudravigilance.ema.europa.eu>, should be included. Standard terms for inclusion of pharmacovigilance for future drugs should be set up, including the upcoming new data protection legislation. Financing agreements is also necessary.

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N. 72

ABSTRACT TYPE

Oral Presentations

TITLE

The I-DSD Registry – A Forum For International Research & Professional Networking

AUTHORS

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ABSTRACT

Background Effective clinical care and research in Disorders of Sex Development (DSD), as well as assessment of long-term outcome of these rare conditions, requires multicentre collaboration across national boundaries and across multiple clinical and research disciplines. Following its inception in 2007, the Registry was initially supported by EUFP7 and, since 2011, has been supported by MRC as the International DSD Registry (I-DSD Registry, G1100236). **Results** In July 2013, there were 1134 cases added by registered users from 22 centres in 15 countries across 3 continents. A further 51 centres from 19 countries covering all 6 habitable continents have registered as users but are not clinical case contributors. The median year of birth of cases entered is 1996 (range 1927-2012). Thus over 50% of cases are now over 16 years old and registered clinicians can contact other clinicians to discuss expert management of similar cases. The commonest disorder type is disorders of androgen action (327) followed by disorders of gonadal development (259). The Registry was upgraded in 2013 and its structure is now an optional modular system for entering clinical data. The Registry supports the development of new primary research through the development of new modules and has also recently completed two projects of secondary research that are based on the existing dataset. This included a review of associated congenital anomalies and a study of trends in sex assignment. **Conclusions** The I-DSD Registry is open to new researchers and clinical contributors who can register to use the Registry at www.i-dsd.org. In addition to acting as a resource for assessing clinical outcome, the I-DSD Registry is facilitating the development of a network of DSD centres and specialists. In case of queries please contact the I-DSD Project Manager, Jillian Bryce (Jillian.Bryce@glasgow.ac.uk).

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ABSTRACT TYPE

Oral Presentations

TITLE

The Lombardy Regional Registry for Rare Diseases: an example of record linkage across different data sources

AUTHORS

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ABSTRACT

Introduction. The Lombardy region, an area of almost 10 million inhabitants in northern Italy, has established in 2007 a regional registry of rare diseases (RD), currently called Registro Lombardo delle Malattie Rare (ReLMaR). The aims of ReLMaR are: - to study the distribution and the characteristics of RD, - to provide guidance for public health policies, - to facilitate clinical research. ReLMaR collects demographic, administrative and clinical data on patients affected by 628 monitored RD, in addition to information about pharmacological therapies. Data are recorded by means of a web-based and smartcard-based software, that allows secure access, exchange and linkage of data. Case definition and data entry are within the competence of medical experts working at Reference Centers appointed by the regional health system. The Coordinating Centre of the RD network is in charge of validation and analysis of data, disseminates periodical reports and sends a shared dataset to the National Center for RD at Istituto Superiore di Sanità in Rome. Although continuously growing, the ReLMaR does not represent to date an effective instrument to fully achieve the expected goals. To better define the regional distribution of RD, ReLMaR data have been recently linked with those coming from the regional administrative database which collects information about the facilities provided to RD patients. **Results.** Overall - until 30 June 2012 - data for 51.987 patients have been collected, of which 49.066 assisted by the regional health system. Patients with RD have been identified by both flows in approximately 21,8% of cases, in 65,3% of cases through the regional administrative database and in 12,9% exclusively through the ReLMaR. Considering the updated information on deceased patients, the prevalence of patients with one of several monitored RD within the Lombardy region can be calculated as at least 46:10.000. Data analysis on updated information (30 June 2013) is ongoing and will allow us to obtain a detailed overview of the distribution of RD at the regional level. **Conclusions.** Linkage of data from several sources provides information not otherwise available, allowing valuable insights into RD epidemiology. Benefits of these linked data include the ability to investigate a broader range of public health questions than with a single dataset.

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ABSTRACT TYPE

Oral Presentations

TITLE

The Eurofever registry: update on enrollment after 3 years

AUTHORS

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ABSTRACT

Background: Autoinflammatory diseases are rare disorders secondary to mutation of genes involved in the regulation of innate immunity. The main limitation to a better knowledge of Autoinflammatory diseases is related to the extreme fragmentation of the diagnosed cases that are spread over different centers and countries. The general aim of the Eurofever Project was to build an international registry on Autoinflammatory diseases. Objective: To evaluate the number of patients enrolled in the registry in the first 24 months after starting the enrolment. Patients and Methods: A web-based registry collecting baseline and cross-sectional clinical information on Autoinflammatory diseases is available in the member area of the PRINTO web-site (www.printo.it). The registry is open to all pediatric and adult Centers with a specific interest in Autoinflammatory diseases. The following monogenic autoinflammatory diseases were considered: Familial Mediterranean Fever (FMF), Cryopyrin-associated periodic syndromes (CAPS), TNF receptor-associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), Blau syndrome, pyogenic arthritis, pyoderma and acne (PAPA) syndrome, deficiency of IL-1 receptor antagonist (DIRA), NLRP12-mediated periodic fever. Information on CRMO, Behçet's disease, PFAPA and undefined periodic fevers were also collected. Results: 2721 patients, from 221 centers in 56 countries, have been enrolled in the registry during the first 36 months. Baseline demographic data (country of residence, disease onset, disease duration, mutations, family history ect) from all patients are now available. In 2213 (81%) complete information on clinical manifestations and responses to treatments is also available. The disease distribution of enrolled patients is: FMF 787 (621 with complete clinical data); TRAPS 237 (211 with with complete clinical data); CAPS 207 (186 with complete clinical data); MKD 153 (133 with complete clinical data); Blau syndrome 62 (21 with complete clinical data); PAPA 19 (18 with complete clinical data); NLRP-12 mediated periodic fever 8 (6 with complete clinical data); DIRA and Majeed 3 and 2 patients, respectively (all with complete clinical data). Among multifactorial autoinflammatory diseases: PFAPA 564 (402 with complete clinical data); CRMO 392 (370 with complete clinical data); pediatric Behçet disease 84 (68 with complete clinical data) and 205 patients with undefined periodic fever (174 with complete clinical data). So far 8 papers involving 56 different authors and 32 centers have been published in high-rank international journals and other papers are in preparation. Conclusions: A large registry of patients with Autoinflammatory diseases is available and, despite the expiring of the initial grant, the enrolment is still ongoing with an increasing number of centers involved. Eurofever represents a good example of how a disease-oriented registry can provide relevant scientific answers to many unknown clinical aspects of ultra-rare diseases. This aspects was the main reason of the relevant success of the enrolment we have observed.



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N. 75

ABSTRACT TYPE

Oral Presentations

TITLE

Spanish Rare Diseases Registries Research Network (Spain-RDR)

AUTHORS

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ABSTRACT

The Spanish Rare Diseases Registries Research Network-SpainRDR is a project financed by the Institute of Health Carlos III (ISCIII) for the years 2012 to 2014. ISCIII is a full member of IRDiRC. SpainRDR aims to build the National Rare Diseases Registry in Spain based on the input of two different strategies: patient registries addressed to patient outcome research and population-based registries addressed to epidemiologic research and social and health systems planning. This project involves all Health Departments of the Autonomous Communities (regions) of Spain, the Spanish Ministry of Health, the Spanish Centre of Reference for People and Families affected by Rare Diseases (CREER), Spanish Medical Societies, four research networks, pharmaceutical and biotechnological organizations (ASEBIO, AELMHU and FARMAINDUSTRIA), the Spanish Federation of Rare Diseases (FEDER) and its foundation (FEDER TELETHON). The Institute of Rare Diseases Research (IIER) acts as coordinator and leader of this network. The project is organised in six work packages: WP1 Coordination and Management, WP2 Registering activity related methods, WP3 Data analysis and outcomes research, WP4 Quality Assessment and ethical and legal issues, WP5 Dissemination and impact, and WP6 Patient registries. The overall gain of the Spanish National Rare Diseases Registry will provide the necessary information to contribute to improve prevention, diagnosis, prognosis and new treatments as well as a better quality of life of patients and their families.

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ABSTRACT TYPE

Oral Presentations

TITLE

ITALIAN CYSTIC FIBROSIS REGISTRY (ICFR) DATA QUALITY ASSESSMENT: CF PULMONARY FUNCTION STATUS

AUTHORS

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ABSTRACT

BACKGROUND Chronic progressive lung disease is the most prominent cause of morbidity and death in patients with cystic fibrosis (CF), but severity of lung disease and rate of lung function decline are widely variable. Pulmonary function data from a CF registry could contribute to understand in which patients this lung function decline is more or less fast. **METHODS** Pulmonary function measures in the ICFR are FEV1, FVC, FEF25-75 (volume and % predicted). We searched for errors in pulmonary function data. **RESULTS** 25 Italian CF Centres contributed to the ICFR database. In 2010 3388 CF patients were treated in these CF care centres. In this analysis the following types of errors affected pulmonary function data: - error type A: FEV1, FVC volumes in millilitres and not in litres. 4/25 (16%) CF centres are affected by this type of error (range: 0.6% - 87.3%) - error type B: FEV1, FVC (% predicted) = 0. 5/25 (20%) CF centres are affected by this type of error (range: 0.6-70.1%) - error type C: FEV1, FVC incomplete: 6/25 (24%) CF centres are affected by this type of error (range: 1.0% - 34.5%) - error type D: non-homogeneous pulmonary function values (0, 1, 2 decimal numbers): 5/25 (20%) CF centres are affected by this type of error (range: 0.5% - 23.5%) - error type E: FEV1 and FVC volume (L) and FEV1, FVC (% predicted) inverted: only 1/25 (4%) CF centres is affected by this type of error. **DISCUSSION** These type of errors could be due to inaccuracy or imprecision in the collection and input of the data in the registry or to a lack of lack of shared rules for allocating data. **CONCLUSIONS** In the next future it will be necessary to understand how to reduce or avoid these errors. Some corrective actions could be planned: train health care professionals involved in the collection and input of data, create a centralized help-desk, continue to audit data entries, learn from data report, define rules for allocating data, etc. **ACKNOWLEDGEMENTS** The authors would like to thank all participants from the 25 Italian CF centres who contributed data. **SUPPORT STATEMENT** The study was supported by Lega Italiana Fibrosi Cistica - onlus.

ABSTRACT TYPE

Oral Presentations

TITLE

ITALIAN CYSTIC FIBROSIS REGISTRY (ICFR) DATA QUALITY ASSESSMENT: CF NUTRITIONAL STATUS

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ABSTRACT

BACKGROUND International guidelines on nutritional interventions in cystic fibrosis (CF) patients emphasized that continuous anthropometric and biochemical monitoring of nutritional status with regular instruction of patients regarding food and dietary supplement requirements is essential for maintaining normal growth and preventing nutritional deficiencies. Anthropometric indicators in a CF registry are essential to determine growth status and to identify malnutrition. **METHODS** Anthropometric measures in the ICFR are height, weight and age. The software calculated other nutritional status variables (BMI, BMI centile, height for age z-score, etc). We searched for errors in anthropometric data. **RESULTS** 25 Italian CF Centres contributed to the ICFR database. In 2010 3388 CF patients were treated in these CF care centres. In this analysis the following types of errors affected nutritional status data: - error type A: anthropometric and pulmonary function parameters are not collected in the same day. 24/25 CF centres are affected by this type of error (range: 1.5-100%) - error type B: wrong weight/height; weight and height reversed. 8/25 CF centres are affected by this type of error (range: 0.3-2.6%) - error type C: weight without decimal numbers: 25/25 CF centres are affected by this type of error (range: 3.8-100%) - error type D: incomplete data: 7/25 centres are affected by this type of error (range: 0.5-11.7%) - error type E: height/weight = 0: 2/25 centres are affected by this type of error (range: 2.3%-31.2%) **DISCUSSION** These type of errors could be due to inaccuracy or imprecision in the collection and input of the data in the registry. **CONCLUSIONS** In the next future it will be necessary to understand how to reduce or avoid these errors. Some corrective actions could be planned: train health care professionals involved in the collection and input of data, create a centralized help-desk, continue to audit data entries, learn from data report, etc. **ACKNOWLEDGEMENTS** The authors would like to thank all participants from the 25 Italian CF centres who contributed data. **SUPPORT STATEMENT** The study was supported by Lega Italiana Fibrosi Cistica - onlus

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ABSTRACT TYPE

Oral Presentations

TITLE

ITALIAN CYSTIC FIBROSIS REGISTRY (ICFR): DATA COMPLETENESS QUALITY ASSESSMENT

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ABSTRACT

BACKGROUND Many disease registries are affected by a lot of missing data. Therefore we sought to examine missing data relative to sweat test, CFTR mutations, PERT therapy, FEV1, FVC, height and weight. **METHODS** ICFR data quality control started in August 2012 and was performed by one informatics and one CF specialist. For the current study 2010 CF patients' clinical and laboratory data were considered. **RESULTS** 25 Italian CF Centres contributed to the ICFR database. In 2010 3388 CF patients were treated in these CF care centres. Fig. 1 and 2 show the results of the completeness analysis. **DISCUSSION** Results of this study show high percentage of missing data for diagnostic data (sweat test, genotype, PERT therapy) and for follow-up data (FEV1, FVC, weight and height). We verified that errors are due to two main reasons: export data procedure and adult patients diagnosed in another CF centre during childhood. **CONCLUSIONS** This study contributed to evaluate the pitfalls of this disease registry. We need to improve the software system in use, reinforce the centre compliance, standardize data collection, etc. **ACKNOWLEDGEMENTS** The authors would like to thank all participants from the 25 Italian CF centres who contributed data. **SUPPORT STATEMENT** The study was supported by Lega Italiana Fibrosi Cistica - onlus.

ABSTRACT TYPE

Oral Presentations

TITLE

ITALIAN CYSTIC FIBROSIS REGISTRY (ICFR) DATA QUALITY ASSESSMENT: CF DIAGNOSIS

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ABSTRACT

BACKGROUND The diagnostic label is essential for a disease registry because some information regarding, for example mortality and survival, could be affected by the contribution of classic disease forms or even atypical disease forms that coexist in CF care centres. **METHODS** In the ICFR each patient is labelled as classic CF or CFTR related disease that doesn't fulfil the diagnostic criteria (1,2). **RESULTS** 25 Italian CF Centres contributed to the ICFR database. In 2010 3388 CF patients were treated in these CF care centres. In this analysis the following types of errors affected diagnosis data: - error type A: patients labelled as pancreatic insufficient don't receive PERT therapy - error type B: PERT therapy = null or unknown - error type C: wrong diagnostic label - error type D: sweat chloride = 0 - error type E: wrong genotype Atypical CF forms are followed-up only in 10/25 CF care centres (range: 0,3-19,6%). **DISCUSSION** The types of errors found could seriously affect the information from a disease registry. Some CF centres didn't indicate the presence of CFTR related diseases and this may be due to a lack of knowledge of the inclusion criteria. **CONCLUSIONS** These results highlighted the importance of quality assessment of a disease registry data that should be preliminary to every observational study. We need some important interventions: improve the level of training of health professionals who enter data in the registry, improve the validation step of data entry, improve the standardization of data entry (CFTR mutation check list, etc). **ACKNOWLEDGEMENTS** The authors would like to thank all participants from the 25 Italian CF centres who contributed data. **SUPPORT STATEMENT** The study was supported by Lega Italiana Fibrosi Cistica - onlus

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